



# The New England Journal of Medicine

Formerly The Boston Medical and Surgical Journal

Established 1828

Published by the Massachusetts Medical Society Under the Jurisdiction of  
The Committee on Publications

VOLUME 223

JUNE-DECEMBER 1940

8 Fenway, Boston

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## KEY TO ABBREVIATIONS

br — book review  
c — correspondence  
cr — case record

— editorial  
MMS — Massachusetts Medical Society  
me — medical eponym

mr — meeting report  
mk — in italics  
— notice

o — obituary  
— original article



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CASE RECORDS  
OF THE MASSACHUSETTS GENERAL HOSPITAL  
ANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT  
TRACY B. MALLORY, M.D., *Editor*

VOLUME 26  
1940





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# The New England Journal of Medicine

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VOLUME 223

JULY 4, 1940

NUMBER 1

## HEMANGIOMA OF THE UTERUS TREATED WITH ROENTGEN RAYS\*

### Report of a Case

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UNUSUAL lesions often stimulate great interest and occasion much speculation as to treatment. It is with this in mind that a case of hemangioma of the uterus is presented. This lesion is rare. It was encountered only once in over 1100 consecutive hysterectomies in the Peter Bent Brigham Hospital during a period of twenty five years. A review of the literature is given by Horgan,<sup>1</sup> who in 1930 reported 1 case, together with 20 collected from the literature. Sixteen additional cases have been reported<sup>2-12</sup> making a total of 38 cases on record.

### CASE REPORT

A 34-year-old married white woman was admitted to the Peter Bent Brigham Hospital on August 17, 1931, complaining of profuse vaginal bleeding of 3 months duration. The previous menstrual history presented no abnormal episodes. The menarche occurred at 15 years of age, with subsequent catamenia of 3 to 4 days duration every 28 days. There had been no menorrhagia, metrorrhagia or dysmenorrhea. The only pregnancy was terminated by a normal uncomplicated delivery of a full term infant, 3 years before entry. Other than an attack of lobar pneumonia, complicated by empyema and necessitating a right thoracotomy 2 years before entry, the patient had always been in excellent health.

The last normal period occurred 4 months before entry. The following period, 1 month later, was prolonged to 10 days but the daily bleeding was normal in amount. On June 1, 1931, 2 months before admission, the patient had a profuse menstrual period of 10 days duration. From that time until her admission she bled persistently with frequent profuse uterine hemorrhages. Associated with this bleeding she had been aware for 3 months of a mass in the lower abdomen, progressive weakness and a heavy dragging sensation in the pelvis.

On physical examination the patient was found to be a well-developed and well-nourished pallid woman. There was a well-healed thoracotomy scar on the chest. The

lungs were resonant throughout with no evidence of residual disease. The heart was of normal size, and the sounds were of good quality with normal rate and rhythm. The blood pressure was 110/60. The abdominal examination was negative except for the presence of an irregular firm mass rising about 5 cm. above the symphysis in the midline. On pelvic examination the suprapubic mass was contiguous with a normal cervix and was freely movable without tenderness. The adnexa were normal.

Laboratory studies revealed grossly bloody urine (voided specimen) with a specific gravity of 1.024, a very slight trace of albumin and sediment containing innumerable red blood cells. The white-cell count was 5900, the hemoglobin 60 per cent (Sahli) and the red-cell count 3,216,000. Blood Hinton and Wassermann tests were negative.

With a preoperative diagnosis of fibroid uterus, on August 18, 1931, under Avertin-ether anesthesia, a supra-cervical hysterectomy, bilateral salpingectomy, left oophorectomy and incidental appendectomy were done. The uterus was irregular firm in most part, but showed some definite softening on the posterior wall which was assumed to be a degenerating fibroid. The uterus was amputated at its junction with the cervix and the cervix closed with interrupted sutures. There was not sufficient reflected peritoneum, however, to cover the raw surface of the cervical stump; the omentum was brought down to the operative field, but was not fixed to the cervix. The wound was closed in four layers.

The postoperative course was uneventful. There was no vaginal bleeding; the urine showed only a rare red blood cell by the 7th postoperative day and no discharge on the 17th postoperative day; the cervix was well suspended and the parametrial tissue normal.

Pathological studies of the removed specimen showed a moderately enlarged uterus, 12.0 by 12.5 cm., with several nodular masses bulging through the external surface which were smooth with reddish-purple, well-circumscribed discolorations. On opening the uterus the endometrial cavity was seen to be displaced well to the left, and bulging into the lumen there were several large, purplish-red polypoid masses which extended down to the external os. The remainder of the endometrium was smooth and of normal color. The cut surface of the myometrium presented small, irregularly shaped, well-circumscribed purplish-red areas, and some brownish red areas which were hemorrhagic in appearance. Though the cut surface bulged slightly there were no fibroids. Both tubes were normal in appear-

From the Surgical Clinic of the Peter Bent Brigham Hospital, Boston.  
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ice The ovary was cystic and only slightly larger than normal, the cysts containing clear fluid

The histological examination of stained tissue showed diffusely invading hemangioma with many intravascular extensions. The section taken through the site of amputation showed that the tumor had not been completely removed. The increased thickness of the uterine wall was due largely to invasion by the hemangioma, which spread apart the fibromuscular bundles of the myometrium. There was no sclerosis of the tumor elements. Small hemorrhages were seen in the large, solid masses of minute

the cervix. It appeared that in endeavoring to free the tumor there was grave risk of injuring the blood supply of the bowel, since there was no line of cleavage. The tumor was firmly fixed against the left lateral pelvic wall, as well as to the base of the broad ligament and the right side of the cervix. It was evident that the tumor was invading the contiguous structures. After prolonged dissection, involving a great deal of bleeding, it was concluded that the lesion was inoperable. Toward the base of the cyst there were a number of rounded, elastic, bluish or purplish tumor masses sprouting into the lumen of the main cyst. A specimen from this area was taken for biopsy.

The microscopic examination of the tissue from the cyst showed the tumor to be composed of masses of innumerable tiny vascular channels, small and irregular sinusoids and numerous small blood vessels, lined by medium sized to small sized endothelial cells which had relatively large nuclei, ovoid to fusiform in shape. The angioma was slowly growing, but in occasional areas appeared to be invasive in type with frequent intravascular extensions.

Following this second operation the patient did well. In the hope that the lesion might prove radio-sensitive, roentgen ray therapy was instituted. On the 12th postoperative day the patient received the first of a series of six high voltage roentgen ray treatments of approximately 400 r each, three anteriorly and three posteriorly to the pelvis. Each treatment consisted of a 20-minute exposure over an area 30 by 30 cm, with 0.5 mm copper and 1.0 mm of aluminum filtration and a target skin distance

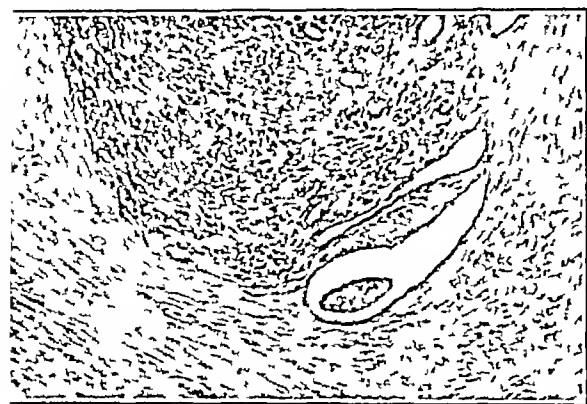


FIGURE 1

*Photomicrograph showing extension of the hemangioma into the myometrium and an intravascular extension below and slightly to the right. Eosin methylene blue stain ( $\times 115$ )*

endothelial lined spaces which composed the tumor. The tubes and ovary were normal microscopically.

The postoperative convalescence was uneventful. The patient was seen in the Outdoor Department, where a cauterization of the cervix was performed which effectively controlled a low grade endocervicitis. There had been no vaginal bleeding, and no symptoms referable to the pelvis. Nine months after the operation the patient began to suffer frontal headaches, which became progressively worse and almost constant. A pelvic examination 1 year after the operation showed a marked increase in the size of the cervix and a contiguous fixed mass about 15 cm in diameter about it. The patient was readmitted to the hospital with the diagnosis of recurrent hemangioma and possible cerebral metastases. Examination of the eye grounds revealed a questionable choking of the left disk. In other respects the examination was negative. Right stereoscopic interoposterior and posteroanterior roentgenograms of the skull showed no localizing signs of tumor or disease. Stereoscopic films of the chest gave no evidence of metastases.

In view of the absence of signs of metastases, removal of an obvious recurrence seemed indicated. The patient was therefore subjected to an exploratory laparotomy on August 6, 1932. On opening the abdomen a round, bluish fluctuating cystic tumor was encountered which filled the basin of the pelvis. An exploration of the upper abdomen showed a normal liver and no evidence of extension or metastases. There were multiple omental adhesions. On releasing these adhesions it was found that the tumor lay between the layers of the mesorectum and mesosigmoid, having pushed itself up out of the pelvis between these layers. It was widely attached by a broad base which apparently sprang from the left aspect of the stump of

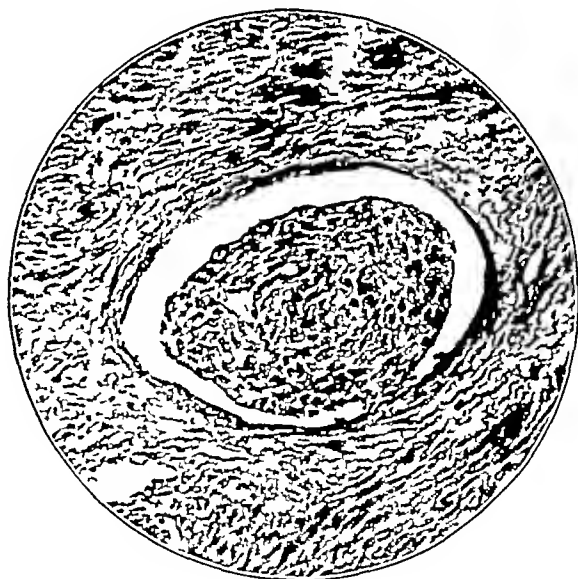


FIGURE 2

*Photomicrograph showing intravascular extension of the tumor in a section of the myometrium removed at the first operation. Eosin methylene blue stain ( $\times 230$ )*

of 40 cm. The last treatment of the series was on August 27, 1932. She was discharged on the 21st postoperative day, August 27, with the wound well healed and the cervix well suspended and fixed. At discharge, there was a fixed, firm mass 7 cm in diameter contiguous with and above the cervix.

The patient was followed in the Outdoor Department. She was symptom free except for a transient attack of edema of the right leg following discharge.

Following a similar series of high voltage roentgen-ray treatments 2 months after operation a rectal examination showed the mass still present above the cervix. The cervix was small and fixed, with smooth induration of the bases of both broad ligaments. After a third series of six roentgen-ray treatments of 400 r each 5 months post-operatively a pelvic examination showed the supracervical mass had disappeared the firm smooth thickening of the bases of the broad ligaments was unchanged, and the cervix was still fixed. The body weight was 145 pounds.

A final course of six roentgen-ray treatments was given 15 months postoperatively. Other than some transient edema of the left leg following these treatments there were no complications. The patient continued in good health with no complaints, maintaining her weight and living a perfectly normal life.

When seen in August, 1938 6 years after the second pelvic operation the patient appeared well and did not complain of discomfort. The body weight was 144 pounds. The lungs were resonant throughout. Abdominal examination showed a diffuse area of fibrosis and edema of the

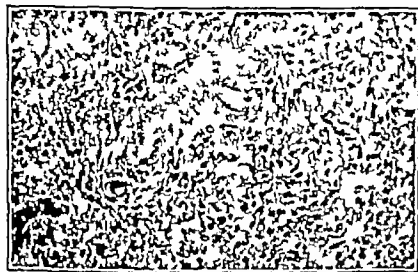


FIGURE 3.

Photomicrograph showing a portion of the recurrence of the hemangioma which was removed at the second operation. Eosin-methylene-blue stain ( $\times 210$ )

suprapubic skin, with many of the typical telangiectases which are seen following high-voltage roentgen ray therapy. This area extended upward for a distance of about 10 cm. Similar telangiectases were noted on the buttocks, but edema and fibrosis were absent. Pelvic examination showed the small firm cervix to be high in the vaginal vault, fixed between the markedly thickened bases of the broad ligaments. No masses could be felt. Stereoscopic roentgenograms of the thorax and pelvis showed no evidence of metastases to lungs or bone and no tumor masses.

While hemangioma of the uterus is a rare condition, the ability to recognize the lesion when encountered will aid the surgeon materially in carrying out the form of treatment that offers the best chance of cure. Of the cases reported relatively few have been associated with alarming symptoms. However, the case herein presented and the cases reported by Siegel,<sup>16</sup> Reder,<sup>17</sup> Horgan,<sup>1</sup> Boldt,<sup>18</sup> and Bokk<sup>19</sup> were associated with serious hemorrhage making surgical intervention imperative. In 2 cases—that reported by Pantzer<sup>15</sup> and the one reported above—there was severe

hematuria. It is obvious that many other pathologic lesions would produce the same symptoms. The diagnosis, then, can be made only at operation. Any spongy, soft, purplish areas or tumors which exude old blood should arouse suspicion.

Hysterectomy has been a satisfactory procedure for treating those cases in which the tumor has not involved other pelvic organs. However, as demonstrated by this case, complete extirpation of the uterus must be done if the tumor involves the cervix. In the treatment of uterine hemangiomas that involve pelvic structures beyond the confines of the myometrium, it is apparent that the danger of hemorrhage and severe injury to the involved organs presents a difficult problem if surgical removal of the tumor is attempted. Ligation of the vessels, individually or en masse, does not preclude the possibility of secondary hemorrhage or recurrence. The successful outcome of this case establishes the fact that the use of high voltage roentgen ray therapy is the treatment of choice for these rare but extensive pelvic tumors. Hemangioma of the uterus, therefore must be added to the list of radio-sensitive tumors in the pelvis.

#### SUMMARY

A case of hemangioma of the uterus is presented with a successful result following deep roentgen ray therapy.

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## THE PREVENTION AND CONTROL OF TUBERCULOSIS IN MASSACHUSETTS\*

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**T**HE trend in the death rate from tuberculosis fortunately continues downward. In the United States for the year 1938 the rate was 48.6 per 100,000 and in Massachusetts 34.7 for the pulmonary and 3.1 for the extrapulmonary forms of tuberculosis, or 37.8 for all forms of the disease. For 1939 in Massachusetts the rate for the pulmonary form of the disease was 33.8, for extrapulmonary forms 2.2, or 36.0 for all forms.

### TUBERCULOSIS IN MASSACHUSETTS

It is important to present the tuberculosis situation in Massachusetts somewhat more in detail and to consider its bearing on the prevention and control of the disease. I am indebted to Dr. Philip E. Sartwell,<sup>1</sup> assistant director, Division of Tuberculosis, Massachusetts Department of Public Health, for the statistical data on death rates, facilities and costs.

Tuberculosis is still a major public-health problem in Massachusetts and in 1939, with 1602 deaths, ranked seventh as a cause of death, but this number of deaths, large as it is, does not serve to measure the full significance of the disease.

Tuberculosis is the leading cause of death in the State at the most productive period of life. More persons between nineteen and thirty-five years of age succumbed from tuberculosis than from any other single cause in 1938. The death rate from the pulmonary form of the disease in this age group rises to about 40 per 100,000 population and tends to rise still higher in the remaining years of life.

The relative importance of the pulmonary form of the disease is increasing and that of the extrapulmonary form diminishing. In 1921, deaths from pulmonary tuberculosis comprised about 83 per cent and those from extrapulmonary forms about 17 per cent. In 1939, the figures were 94 and 6 per cent respectively. Though extrapulmonary tuberculosis is frequently secondary to pulmonary lesions, infected milk is a factor. Elimination of the disease in cattle and pasteurization of milk are largely responsible for the diminishing proportion of deaths from extrapulmonary tuberculosis. To

eliminate the chance of human infection from tubercle bacilli or other organisms in milk, all milk should be pasteurized.

The spread of tuberculosis is more readily prevented in institutions than in the home, and it is of interest to note that in 1938 about 80 per cent of the deaths from the disease occurred in institutions and only about 20 per cent in the home. For the benefit of the individual, and the protection of the family and the community, patients with tuberculosis should be urged to go to institutions.

The degree to which tuberculosis is a menace is not the same in all counties in the State. In general, those counties having the highest density of population have the highest death rates. Over a five-year period (1935-39), excluding the counties of Dukes and Nantucket because of their small populations, Suffolk County had the highest death rate, 57.2, and Franklin County the lowest, 20.1 §.

### FACILITIES

The facilities in 1939 for patients with tuberculosis in Massachusetts comprised 4522 beds in federal, state, county, municipal and private institutions, a ratio of beds to deaths in 1939 of 2.8:1.

Diagnostic clinics under official auspices are available throughout the State. Diagnostic outpatient departments are maintained at the state and county sanatoriums, and through extension of their facilities there are twenty-three extramural consultation clinics, for the most part located in outpatient departments of general hospitals and with x-ray facilities available.

In addition, there are thirty-nine tuberculosis dispensaries, conducted by local boards of health. X-ray facilities, though indispensable, are lacking in these dispensaries except in a few of the larger communities, and it is desirable, as recommended by the Massachusetts Health Commission (House Bill No. 1200, p. 74), that all communities except those with approved tuberculosis hospitals be encouraged to arrange with the state and county sanatoriums for tuberculosis diagnostic service and to discontinue their locally staffed clinics.

### COSTS OF TUBERCULOSIS

Facilities for tuberculosis in Massachusetts were maintained at an estimated cost in 1938 of

\*The presidential address delivered at the annual meeting of the Massachusetts Tuberculosis League at the Middlesex County Sanatorium, Waltham, Massachusetts, March 25, 1940.

†Clinical professor of medicine, emeritus, Harvard Medical School; member, Board of Consultation, Massachusetts General Hospital, Boston.

§Figures corrected for residence.

\$5,106,238 17, not including federal contributions, expenses of local health departments in case finding, supervision of patients in the home, maintenance of dispensaries and other related costs

#### EXAMINATION OF SCHOOL CHILDREN

Clinics under the auspices of state and county sanatoriums for the school year 1938-39 covered a high school population of 53,285 children, of whom 34,897 (65 per cent) were tuberculin-tested. The proportion investigated is dependent on parental consent and, strange as it may seem, it has seldom been possible to test more than about two thirds of the children.

Clinics under other auspices covered a school population in one city of 19,351, of whom 10,202 (53 per cent) were tuberculin tested, and in another city 1215, of whom only 244 (20 per cent) were tuberculin-tested. Failure to investigate a larger proportion of the children may be taken in part as a measure of the shortcomings of the tuberculosis associations in health education.

In a total school population of 73,851 children 45,343 (61 per cent) were tuberculin-tested and 9730 (21 per cent) gave positive reactions. In the course of the investigation, 12,503 children were x-rayed. Forty-four cases of the adult type of tuberculosis were found, or about 1 for every 1000 tuberculin tested children and 1 for every 221 reactors. The childhood type of tuberculosis was discovered in 1083 children, or 1 in every 42 tuberculin tested and 1 in every 9 reactors.

#### SCHOOL PROGRAM

The routine examination of school children is an expensive project. Estimating the cost at \$100 to \$150 per child tested with tuberculin, the expense of finding each case of the adult type of tuberculosis in a child amounts to between \$1000 and \$1500.

The adult type of tuberculosis in children is serious and the outlook is poor. It is of great moment to make the diagnosis early and resort at once to appropriate treatment. The childhood type, on the other hand, is usually mild and the outlook favorable. Its discovery is to be regarded as an indication for certain precautions and further observation by x ray.

In communities where the case finding program both in and outside the schools is well developed and a large proportion of the contacts of all known cases are examined by x ray, the chance of finding a previously undiscovered case of the adult type of the disease in a school child is much diminished. The per capita cost of finding such a case is, in consequence, much increased.

It would seem, therefore, that in communities where the case finding program among contacts is well developed and funds are limited, the routine investigation of all contacts is to be preferred to the investigation of school children when a choice of methods must be made.

#### INVESTIGATION OF CONTACTS

An important present responsibility of the tuberculosis associations is the promotion of the new rules and regulations of the Massachusetts Department of Public Health.<sup>2</sup> Under these regulations, as soon as a diagnosis of tuberculosis has been established, arrangements should be made for the examination, including an x ray of the chest, of all members of the immediate family and of other persons with whom the patient has been in close contact.

Examination of family and other contacts has the advantage of a higher proportion of positive findings than is obtained in other groups in the community, and offers the opportunity of benefit to the individual through the application of appropriate treatment and to the family and the community by the breaking of contact. If the family cannot afford an x-ray examination by a private physician, facilities are fortunately available through the state, county and municipal sanatoriums.

#### CASE FINDING IN OTHER GROUPS

It is desirable that certain groups be routinely investigated. Nursemaids and other domestic servants in homes where there are children should have an x ray examination prior to employment for the purpose of protecting those with whom they come in contact. All school teachers and other employees in contact with children should be examined for tuberculosis for the protection of children.

With respect to the investigation of school teachers, attention may be called to the appeal to the Massachusetts Tuberculosis League to formulate suggestions for school departments and the recommendation adopted at the directors meeting of the League on March 30 1939, as follows:

It is recommended that school authorities require prior to employment and at suitable intervals thereafter the examination by x ray and other accepted procedures, of all teachers and other employees in contact with children in the public and private schools. No teacher or employee with active pulmonary tuberculosis or any form of tuberculosis which may endanger the health of the children will be permitted to teach or continue in employment. The x ray examination shall be made at an x ray laboratory approved by the school committee. Examination is to be made by a physician or physicians designated or approved by the school department and be free of expense to the person examined.

Arrangements may be made by the school department for such examinations by the staffs of the state or county sanatoriums

The school boards of thirty-four communities in Massachusetts have adopted this recommendation or have a similar regulation in effect. In this connection, it may be noted that periodic examinations for tuberculosis of pupils, teachers and employees in public schools is now required by law in New Jersey.<sup>3</sup> Pupils who fail to comply with this requirement and pupils with tuberculosis in a communicable form are excluded from schools.

Medical students, student nurses and interns in hospitals are more intimately exposed to tuberculosis than are those in other occupations, and should in consequence be routinely examined.

From an inquiry conducted by the League relative to the practice of examination of nurses, it was found in returns from sixty of sixty-seven training schools that an x-ray examination is done annually on all students in thirty-two, and twice during the course in six. In the remaining twenty-two training schools no x-ray examination is made at any time.

In view of the increased hazard to nurses from tuberculosis and the importance of its early discovery, the Executive Committee of the Massachusetts Tuberculosis League voted to submit the following recommendation to the Executive Committee of the Massachusetts Hospital Association:

It is desirable in the opinion of the Executive Committee that there be a chest x-ray examination annually, or oftener if necessary, of student nurses and all other hospital personnel in contact with patients, and including food handlers. The first examination should be made about the time of beginning employment.

#### RESPONSIBILITY OF LOCAL BOARDS OF HEALTH

According to the rules and regulations of the Massachusetts Department of Public Health, "it is the responsibility of the local board of health to provide hospital care for cases of tuberculosis, when needed, and to see that contacts are examined where such examination cannot be made through a private physician." It is to be expected that the local tuberculosis associations can be of assistance to local boards of health in promoting that part of this regulation which has to do with the examination of family contacts.

#### COMMUNITY RESPONSIBILITY FOR RELIEF

In carrying out these regulations economic factors must not be permitted to stand in the way of proper treatment for the individual and the protection of the family and the community. Means must, if necessary, be provided from public-welfare or social-welfare agencies adequately to meet the

needs of the family occasioned by illness from tuberculosis.

In this connection, attention may be called to the principles under which the tuberculosis associations operate. It is not their function to provide relief out of Christmas Seal funds. It is their function to encourage adequate relief by appropriate agencies, but beyond this they should not go, except in an emergency and as a temporary expedient.

#### RESPONSIBILITIES OF THE TUBERCULOSIS ASSOCIATIONS

It has seemed desirable to the Executive Committee of the League to consider how, under changing conditions, the associations can use their funds to the best advantage. A recently formulated interpretation of the pamphlet *Authorized Forms of Tuberculosis Work*,<sup>4</sup> has been published.<sup>5</sup>

The Executive Committee plans to survey the activities of the local tuberculosis associations, give attention to their special problems and, so far as possible, assist them in planning and conducting a program for the prevention and control of tuberculosis in their communities.

Detailed comment on the desirable activities of the associations is unnecessary, but certain aspects may be emphasized. The chief concern of the voluntary associations is the formulation of a well-rounded program in accord with local needs and in co-operation with official agencies. Full-time trained workers are necessary for the accomplishment of these purposes and, where lacking, should be secured. Funds for this purpose should, if necessary, be made available through a change of policy with respect to the allocation of receipts from the Christmas Seal sale. At present in many communities large proportions of these funds go toward the support of summer health camps. In some communities considerable proportions are distributed to local tuberculosis committees to supply milk for tuberculous families and school children, dental service and tonsillectomies. These funds can be used to better advantage for health education, for the promotion of case-finding, hospitalization and the breaking of contact, for rehabilitation, and for the investigation of local tuberculosis needs.

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## MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND  
FIFTY NINTH ANNIVERSARY

THE one hundred and fifty ninth anniversary of the Massachusetts Medical Society was observed in Boston, Tuesday and Wednesday May 21 and 22, 1940. The headquarters were located at the Copley Plaza Hotel where all scientific meetings were held and exhibits were shown.

## FIRST DAY MAY 21

A general clinical meeting was held in the Sheraton Room in the forenoon under the chairmanship of Dr. A. Warren Stearns. The attendance was 228.

The supervising censors met in Parlor A at 10:00 a.m. and the Council was convened in the Swiss Room at 10:30. The Copping Luncheon was served at 1:00 p.m.

During the noon hour there was a series of section round-table meetings and luncheons at which the new officers were chosen (see Appendix).

The Section of Medicine met in the President's Room of the University Club, the attendance was 89.

The Section of Obstetrics and Gynecology held its meeting in the Main Dining Room of the University Club, there was an attendance of 144.

The Section of Surgery met in the Crystal Room of the Westminster Hotel, with an attendance of 50.

The Section of Pediatrics held its meeting in the Ballroom of the Westminster Hotel, the attendance was 70.

The Section of Dermatology and Syphilology met in the State Salon of the Copley Plaza, with an attendance of 50.

In the afternoon a general clinical meeting and symposium on respiratory tract infections was held in the Sheraton Room under the chairmanship of Dr. William H. Robey. The attendance was 388.

The annual dinner was held in the Main Dining Room at 7:00 p.m. The attendance was 264. During the dinner the President presented the newly elected officers and the guests at the head table. He next presented the delegates from the other New England state medical societies as follows:

MAINE: Dr. Thomas A. Foster, Portland  
NEW HAMPSHIRE: Dr. George V. Fiske, Manchester  
Dr. Addison Roe, Newport  
VERMONT: Dr. Roland E. McSweeney, Brattleboro

RHODE ISLAND: Dr. George L. Young, East Greenwich  
CONNECTICUT: Dr. Walter C. Haviland, Mansfield  
Dr. Edward J. Ottenheimer, Willimantic

Following the dinner Dr. Ernest W. Goodpasture presented the Shattuck Lecture in the Sheraton Room. The subject was Immunity to Virus Diseases. Some theoretical and practical considerations (published in the *Journal* issue of May 30). The attendance was approximately 575.

## SECOND DAY MAY 22

In the forenoon a general clinical meeting and symposium on syphilis was held in the Sheraton Room under the chairmanship of Dr. C. Guy Lane. The attendance was 400.

## ANNUAL MEETING

The annual meeting of the Society was called to order by the president Dr. Walter G. Phippen, of Salem, at 11:00 a.m. There were approximately 400 in attendance. The minutes of the one hundred and fifty-eighth meeting of the Society were approved as published in the *New England Journal of Medicine* issue of July 6, 1939. The Secretary then presented the changes in membership as follows:

Membership reported June 8, 1939	5438
Less member who was not restored since he failed to meet his financial obligation	1
	<hr/> 5437

Losses	
Deaths	99
Resignations	23
Deprivations	38
	<hr/> 160

Gains	
New fellows	252
Readmitted by censors	3
Restored by Council	10
	<hr/> 265

Net gain	105
Membership reported May 22, 1940	<hr/> 5542

The Secretary announced that the New England Postgraduate Assembly would be held in Sanders Theatre and Memorial Hall, Harvard University, on Wednesday and Thursday, November 13 and 14, 1940. There is an impressive list of speakers. The committee in charge hopes to

House, a Salem garden and luncheon at the Salem Country Club

The Golf Tournament, under the chairmanship of Dr William T O'Halloran, was held at the Belmont Country Club on Tuesday, May 21. There were twenty-two players. The distribution of prizes was as follows:

Low net (Burrage Bowl) — Dr Oliver A Lothrop  
 Second low net — Dr John W Henderson  
 Third low net — Dr Thomas J Cavanaugh  
 Low gross — Dr Richard S Nugent  
 Second low gross — Dr Robert Dutton  
 Third low gross — Dr Joel M. Melick

The total registration for the two-day meeting was as follows:

Physicians	1461
Ladies	200
Total	1661

The lists of admissions and deaths are appended, together with the official lists of officers, standing and special committees, councilors, censors and so forth.

## APPENDIX

### ADMISSIONS RECORDED FROM JUNE 8, 1939 TO MAY 22, 1940

YEAR OF ADMISSION	RESIDENCE	MEDICAL COLLEGE
1939	Adams, Ralph Hudson, Cambridge	11
1939	Aieta, Joseph, Jr, Dorchester	10
1940	*Allendorf, Francis Jasper, Walpole	6
1940	Alpert, George Roland, Brookline	45
1940	Altschule, Mark David, Boston	11
1939	Anderson, Leonard Edward, Longmeadow	38
1938	†Arey, Jean McIntosh, Gardner	12
1940	Arnold, Jesse Oglevee, 2nd, Worcester	2
1939	Aufranc, Otto Elmo, Brookline	11
1940	Baldwin, Albert Kilburn, Taunton	46
1940	Baldwin, Arthur Dwight, Wellesley	11
1940	Baldwin, Gertrude W, Cambridge	47
1940	Barbour, Charles Manson, Jr, Newton Highlands	9
1939	Barker, Robert Howard, Waban	11
1940	*Beer, Peter Johann Otto, Waltham	48
1939	Beigelman, Herman, Roxbury	12
1940	*Benda, Clemens Ernst, Wrentham	49
1940	Benson, Harry Ludvig, Winchester	10
1940	Berezin, Martin Arthur, Harding	10
1939	Bergman, Micks Leonard, State Farm	7
1939	Persack, Solomon Rodney, Springfield	3
1939	Blaisdell, John William, Lawrence	12
1940	Blaney, Cyril Arthur, Westford	10
1939	*Bloom, Philip, Somerville	8
1940	Blouin, Alfred Rodolph, Northbridge	10
1940	Blum, Max, New Bedford	50
1940	Bonner, Hugh Joseph, Jamaica Plain	9
1939	Bradley, Joseph Augustine, Lawrence	12
1939	Brenner, Charles, Brookline	11
1939	Brinegar, Willard Clouse, East Gardner	16
1939	Brines, John Kincaid, Wellesley	11
1939	Bryant, Mason David, Jr, Lowell	12
1939	Buddington, Weston Turner, Newton	11
1939	Bush, Charles William Jr, Milton	10
1939	Casa, Pasquale Conrad, Springfield	12
1940	Cannon, Bradford, Cambridge	11
1940	*Canzanello, Vincent Joseph, Everett	6
1939	Carbone, Joseph Alfred, Springfield	15
1939	Carleton, Thomas McMaster, Brookfield	12
1940	*Carmody, Robert Fulton, Brookline	6
1939	Cass, Leo Joseph, Cambridge	11
1940	Chafetz, Max, Dorchester	12
1939	Cheever, Francis Sargent, Wellesley	11
1939	Chiminello, Frank Joseph, Quincy	10
1940	Chippendale, Francis David John, Fall River	19
1940	Clarke, Samuel Tracy, Boston	11
1939	Cogan, Michael Aaron, Holyoke	14
1939	Coggeshall, Howard Cranor, Boston	36
1939	Cohen, Jack Dexter, Brookline	12
1939	Cohen, Samuel Louis, Boston	10
1940	*Colantino, George Joseph, Malden	6
1939	Colcock, Bentley Prescott, Jamaica Plain	22
1939	Collins, James Francis, Gloucester	12
1939	Colman, Joseph Harry, Mansfield	12
1940	Comanduras, Peter, Roxbury	12
1940	Commette, Joseph Paul, Beverly	10
1939	*Condo, Annunziato, Lawrence	31
1940	*Conroy, John Albert, Newton	40
1939	Constantian, Harold Martin, Worcester	24
1939	Conway, Christopher Clarence, Malden	12
1939	Cooper, Philip, Brighton	11
1939	Corcoran, John Joseph, Lowell	12
1940	Crandon, John Howland, Boston	11
1939	Crowley, John Joseph, Lynn	11
1940	Cutler, Joseph George, Salem	18
1939	Damiani, Clito Robert, Lowell	12
1940	Davis, Burnet Madura, Boston	11
1939	†Dawson, Raymond J, Methuen	9
1939	Dee, John Foley, Indian Orchard	10
1939	DeNuccio, Adolph Alfred, Lawrence	10
1939	DerHagopian, Ardashes Paul, Chelsea	12
1939	Dickson, Ellsworth Joseph Murray, Needham	12
1939	Dineen, John Bernard, Springfield	19
1940	†Donaghy, George Everett, Boston	12
1940	*Driscoll, Daniel Timothy, Malden	6
1939	Duggan, George Leonard, Lowell	19
1939	Durant, Richard Church, Great Barrington	11
1939	Dynes, John Burton, Boston	11
1940	Elder, Burton F, Hingham	51
1939	Elia, Andrew Dimitri, Boston	10
1940	Ficicchy, John, Jr, Hyde Park	10
1939	Fiman, Charles Elden, Taunton	28
1940	Fine, Jacob Harold, Beverly	12
1940	Finley, Knox H, Brighton	1
1940	*Fischer, Joseph, Brighton	52
1940	*Fishgal, Maurice Charles, South Boston	6
1939	Flo, Spencer Carlyle, Greenfield	38
1939	Forbes, Anne Pappenheimer, Milton	29
1940	Freeman, Rowland Godfrey, Jr, Dover	29
1939	Friedberg, Isadore Hirsh, Brighton	12
1940	Friedman, Emerick, Waltham	53
1940	Fritz, Lewis Edward, Stoughton	12
1939	Fromer, John Lewis, Brookline	4
1939	Frothingham, Joseph Rotch, Boston	11
1940	*Fulder, Hans, Worcester	54
1940	Gahm, Irvin George, Boston	12
1940	Gall, Edward Alfred, Cambridge	50
1939	Garipey, Alonzo Joseph Asias, Barre	12
1940	Gates, Donald Coats, Boston	11
1939	Gibson, John Graham, 11, Cambridge	11

1939	Giddon, Elliot David, Brookline	10	1940	McLaughlin, Joseph <del>Alexander</del> New Bedford	12
1940	Goldman, Max, Boston Harbor	12	1939	Mehan Mona Catharine, Hathorne	44
1940	Gordon, Sydney Raphael, Worcester	12	1940	Meltzer Adolph Worcester	33
1939	Gorney Arthur Joseph Chestnut Hill	12	1940	*Mindus, Walter Valk, New Bedford	62
1940	Gould David Marshall Boston	11	1940	Moore Paul Thomas, Milton	11
1939	Grace, Sydney Cambridge	10	1939	*Moriarty James Edward, Roslindale	6
1939	Grainger James Eldredge, Worcester	12	1940	Moritz, Alan Richards, Waban	16
1940	*Grinold John Joseph Belmont	6	1939	Most, Frank Peele, Jr., Jamaica Plain	12
1940	Gudas, Peter Paul Boston	10	1939	Mulhern John Francis Jr., Taunton	12
1939	Haddad Arthur Kahl Worcester	12	1940	Mullaney, Owen Christopher, Dorchester	10
1940	Hadler, Arthur Joseph Boston Harbor	11	1940	Mushlin Harry Ralph Brookline	10
1939	Haines Solomon Manuel, East Gardner	21	1940	*Nadel Frederick Philip Cambridge	6
1940	Hand, Leo Vincent, Wellesley Hills	2	1940	Nathanson Ira Theodore, Boston	25
1940	Hawkins Ralph Leslie, Boston	11	1940	Nelson, Roy Walter Attleboro	10
1940	Hearne, Thomas Myers Melrose	10	1940	Newton, Aaron Wayne, Boston	12
1940	Hindman Daniel Harold Roxbury	11	1939	Nicholson Morris John Roxbury	39
1940	Hinds, Charles Benjamin, Jr. Worcester	11	1939	O'Brien, Thomas Emmet, Lynn	12
1939	Hirtle, Ralph Benjamin, Malden	11	1939	O'Brien Thomas Joseph, Hudson	12
1939	Hiscock, Mabelle Caroline, Roxbury	18	1939	*Oddy Parkinson Louis, Methuen	6
1938	†Hitchcock, James Fitchburg	63	1939	Olan, Sidney Somerville	10
1939	Holleran Harold Westfield	12	1939	*O'Neill John James, Salem	40
1939	Hooper Langdon Wellesley Hills	11	1939	Orlov, Samuel Warcham	12
1939	Houle, Emile Antonio Lowell	10	1940	Osgood, Rudolf Belmont	15
1940	Hoxie, Thomas Barr Boston	12	1939	Parington Philip Raymond, Great Barrington	29
1939	Huber, William McPherson Brookline	22	1939	Pekala Joseph Gabriel Northampton	7
1940	Hyder, George Abdallah, Lawrence	12	1940	Pelton, Thurlow Hensworth, Pittsfield	11
1939	Hyman, Mayer Boston	15	1940	*Pett, Morris Hinch Gloucester	6
1939	*Jacobs Perry Harry Hudson	6	1939	Philbrook Frank Randolph Randolph	10
1939	Janeway Charles Alderson, Weston	18	1940	Pittman, Merry Elizabeth, Roxbury	15
1939	Johnson Paul Emanuel Attleboro	12	1940	*Pollak, Oskar Jaroslav Allston	56
1939	Joy Genevieve Louise Stonham	28	1940	*Rak, Ian Parley Lexington	57
1940	Kaufman, Manuel Tewksbury	12	1939	Remy, Sylvio Bernard Webster	19
1940	Kaufman, S. Harvard, Worcester	13	1939	Reuter, Robert John Roxbury	35
1940	Keane, Geoffrey Patrick, Fall River	11	1939	Risman Joseph Lynn	7
1940	Kemble, Robert Penn, Worcester	21	1939	Romano, John Boston	35
1940	*Kevorkian John Jacob Watertown	20	1939	Rosenheim, Frederick, Belmont	29
1940	King Marion Alden, Northampton	10	1940	Rozanski Frank Stanley Worcester	58
1940	Kinsey Dera Brookline	41	1939	Salter William Thomas Milton	11
1939	Klainer, Max Joseph Stoneham	10	1940	Saphir Nelson Robert, South Boston	17
1940	*Kotarski William C., Springfield	6	1939	Sargent, Morgan, Quincy	1
1939	Kunkel Paul, Boston	17	1939	Schultz, Philip Ephraim Roxbury	37
1939	Lamb Gordon Richard, Brookline	38	1939	*Scola Joseph Anthony, Worcester	6
1940	Lappin Abraham Henry Dorchester	12	1940	Sellman Priscilla Newton	10
1939	Lathrop Frank Damron, Brookline	38	1939	Senecal Alphonse Leonard Beverly	9
1939	Laughran James Frederick, Lowell	12	1939	Sevall Kenneth Wilkins Boston	11
1939	*Laurin Theophile, Lowell	23	1939	Shlossberg Frank, Lowell	42
1940	Leadbetter Wyland Fenway Brookline	18	1940	Shniber William Jacob Dorchester	38
1939	*Lentuno, Joseph Webster Clinton	27	1939	*Silbert, Nathan Ernest Dorchester	40
1940	*Lever Walter Frederick, Boston	55	1940	*Skrahucha William Albert, Lowell	6
1940	*Levison, Carl Dorchester	6	1939	Slemmons, Marion Lucile, Quincy	38
1940	Lewis, Emil Harold East Boston	10	1939	Smith Edwin Andrew Lynn	12
1939	Lewis, James Westfield	11	1939	Souders, Carlton Remsburg Jamaica Plain	11
1939	Lindberg Theodore Frederik Dorchester Center	25	1940	Spira Bertram Worcester	59
1939	*Lindemann Erich Boston	30	1939	Staples, Oscar Sherwin Hyde Park	12
1940	Lowd, Harry Mosher Jr., Salem	5	1940	Stearns Carl Boston Harbor	12
1939	Lulow William Victor Scituate	12	1939	Steele, George Chapin, West Springfield	11
1940	MacKillop John Angus Cambridge	12	1940	Stevenson Charles Summers	18
1939	MacLaughlin Charles Harland Everett	12	1939	Sullivan Francis Xavier Hathorne	12
1940	*Mauzzo Anthony M Beverly	6	1939	Sullivan Garrett Leo, Jr., Cambridge	11
1940	Malamud, William Worcester	9	1940	Sweetser Frederick Nelson, Roxbury	12
1940	*Malool Frederic, Boston	6	1940	Tate, John Comstock Westfield	60
1939	Manganelli Charles Vincent, Lynn	12	1940	Teahan William Waters Holyoke	22
1939	Manley James Sylvester New Bedford	12	1940	*Thomas John Donofrio, Nahant	20
1939	Markey Hilda Allston	32	1939	Thompson Richard Hildreth Boston	11
1940	†Marvin Frank William West Newton	11	1939	Thornton Joseph Peter Dorchester	10
1939	*Mattia Anthony Francis Fitchburg	20	1940	Tourney James William, Jr., Dedham	29
1939	Mazer Mendel Springfield	29	1940	Tuck, Herbert A., Fitchburg	12
1939	McCarthy Ralph Philip Peabody	19	1940	Twinam Claire Willard, Pittsfield	61
			1939	Vance Lewis Alexander Cambridge	43

1939	Vastine, Mary Frances, Roxbury
1939	*Vohr, Dorothy Larrison, Lee
1940	Warbasse, James Peter, Jr., New Bedford
1939	Warren, Richard, Boston
1940	Warthin, Thomas Angell, Boston
1939	Wisserman, Mitchell, Mansfield
1940	Watkins, Arthur Lancaster, Arlington
1939	Weintrub, David, Brighton
1939	*Wekstein, Abraham Jacob, Mattapan
1939	Whelan, Edmund Lawrence, Malden
1939	Wiener, Harry Julius, Revere
1940	*Willgoose, Dorathea May, Needham
1939	Wilson, Carl, Springfield
1940	*Wissing, Egon Georg, Boston
1939	Wolf, William, Lowell
1940	Wright, Marian Lucia, Boston
1939	Wright, Rebekah, Arlington
1939	*Zalvan, Jacob, Millis
1940	Ziegler, Edwin E., Chelsea
1940	Zoll, Paul Maurice, Boston

Total number new fellows admitted November, 1939	138
Total number new fellows admitted May, 1940	114
Total number fellows readmitted November, 1939	1
Total number fellows readmitted May, 1940	2
Grand total	255

\*The candidate's diploma was approved by the Committee on Medical Education and Medical Diplomas and he or she was given a personal interview by this committee and permitted to take an examination before a board of censors

†Readmitted by censors

‡Omitted from previously published list

#### KEY TO MEDICAL COLLEGES

1	Yale University School of Medicine
2	Temple University School of Medicine
3	University and Bellevue Hospital Medical College
4	New York University College of Medicine
5	University of Rochester School of Medicine
6	Middlesex University School of Medicine
7	University of Vermont College of Medicine
8	Missouri College of Medicine and Science
9	McGill University Faculty of Medicine
10	Boston University School of Medicine
11	Harvard Medical School
12	Tufts College Medical School
13	University of Wisconsin Medical School
14	Vanderbilt University School of Medicine

44	15	Rush Medical College of the University of Chicago
6	16	University of Nebraska College of Medicine
24	17	Washington University School of Medicine
11	18	Johns Hopkins University School of Medicine
11	19	Georgetown University School of Medicine
10	20	College of Physicians and Surgeons, Boston
11	21	Jefferson Medical College of Philadelphia
9	22	University of Pennsylvania School of Medicine
6	23	Baltimore University School of Medicine
12	24	Long Island College of Medicine
38	25	Northwestern University Medical School
6	26	University of Bishop College Faculty of Medicine
43	27	Royal University of Rome
49	28	College of Medical Evangelists
12	29	Columbia University, College of Physicians and Surgeons
10		
25	30	University of Giessen, Germany
6	31	Royal University of Medicine and Surgery, Naples
34	32	University of Toronto Faculty of Medicine
11	33	Cornell University Medical College
	34	George Washington University Medical School
	35	Marquette University School of Medicine
	36	Indiana University School of Medicine
	37	Creighton University School of Medicine
	38	University of Michigan Medical School
	39	University of Maryland School of Medicine and the College of Physicians and Surgeons
	40	Kansas City University of Physicians and Surgeons
	41	Baylor University College of Medicine
	42	Dalhousie University Faculty of Medicine
	43	University of Virginia Department of Medicine
	44	Woman's Medical College of Pennsylvania
	45	University of California Medical School
	46	Medical School of Maine
	47	University of Pittsburgh School of Medicine
	48	Ludwig-Maximilians-Universität, Munich
	49	University of Berlin
	50	Tulane University of Louisiana School of Medicine
	51	Ohio State University College of Medicine
	52	University of Vienna
	53	University of Buffalo School of Medicine
	54	University of Lausanne
	55	Universities of Heidelberg, Vienna, Zurich, Hamburg, Leipzig
	56	Medical School of Masaryk University of Brno
	57	University of Leipzig
	58	Hahnemann Medical College and Hospital of Philadelphia
	59	University of Illinois College of Medicine
	60	University of Tennessee College of Medicine
	61	State University of Iowa College of Medicine
	62	Friedrich Wilhelms University, Berlin
	63	Dartmouth Medical School

#### DEATHS REPORTED FROM JUNE 8, 1939 TO MAY 22, 1940

ADMITTED	NAME	PLACE OF DEATH	DATE OF DEATH	AGE
1895	Abbe, Frederick Randolph	Boston	March 2, 1939	70
1904	Adams, Zabdiel Boylston	Brookline	March 16, 1940	65
1914	Allison, Carl Edwin	Chelsea	June 9, 1939	52
1922	†Bacon, Gorham	Yarmouth Port	March 5, 1940	84
1893	†Bulev, George Guy	Ipswich	March 30, 1940	75
1892	Baker, Frederick Herbert	Worcester	October 1, 1939	72
1898	Berg, Tekla Amalia Josefina	Lynn	June 8, 1939	70
1914	Berry, Charles Francis	Boston	October 10, 1939	68
1904	†Blenkhorn James	Stoneham	October 8, 1939	75
1902	Borden, Charles R. C.	Brookline	November 28, 1939	65
1893	Brewster, George Washington Wales	Boston	September 26, 1939	73

1907	†Brigham Fred Clayton	Springfield	January 22, 1940	69
1892	†Burke, James Joseph	Easthampton	November 16 1939	79
1901	Burnham Joseph Forrest	Boston	January 26 1940	70
1897	Butler, George Edward	Fall River	March 8 1940	71
1918	Callanan Francis Jervois	Boston	April 21 1940	45
1911	Carlisle, Frank Henry	Wellesley	July 20 1939	60
1905	Carroll John Joseph	Holyoke	November 19 1939	61
1933	Cassidy James Michael	West Springfield	October 4 1939	35
1920	Cheney Robert Cartwright	Boston	February 8 1940	45
1905	Chesley, Alfred Ervan	Lawrence	October 27 1939	63
1885	Coolidge, Algernon	Boston	August 16 1939	79
1899	Crandon, LeRoy Goddard	Boston	December 27 1939	66
1892	†Crocker Benton Pulsifer	Foxboro	May 26 1939	72
1913	Cushing Harvey	New Haven Conn.	October 7 1939	70
1887	Cushman, Andrew Bernard	South Dartmouth	February 13, 1940	83
1927	Damsky Charles	Lynn	December 3 1939	45
1906	Davis, Ernest Leland	Springfield	September 10 1939	67
1914 } 1937 }	Dervin Lawrence James	Somerville	March 30 1940	64
1937	Dexter Smith Owen, Jr	New York City	November 25 1939	32
1922	Doherty Henry Leo	Stoughton	October 9 1939	45
1918	Emard George Adelbert	Mansfield	August 3, 1939	57
1906	†Felch Lewis Perley	Boston	April 2, 1940	68
1921	Fitchet, Seth Marshall	Newton Centre	September 26, 1939	52
1906	Gallagher John Henry Connaughton	St. Petersburg Fla.	March 19 1940	57
1914	Gaylord James Frederick	Springfield	June 8 1939	49
1921	Gibson David Howard	Cambridge	June 8 1939	54
1897	Hallett, Edward Bangs	Cloucester	November 8 1939	75
1890	Harding George Franklin	Brookline	May 16 1940	77
1903	Harrington Michael William	Indian Orchard	November 13 1939	66
1898	Hayes Albert Edwin	Edgewood R. I	Unknown	73
1902	Hewitt, William Oakes	Boston	April 27 1940	63
1903	Hillard James Pearse	Springfield	January 29 1940	62
1915	Hiltbold, Werner	Easthampton	April 5 1940	50
1917	†Howard Charles Tilden	Hingham	September 6, 1939	68
1920	Hughes, Frank	North Weymouth	September 13 1939	67
1897	†Irwin Vincent Joseph	Tampa Fla	June 19 1939	84
1919	Jordan, Michael Matthew	Worcester	September 30 1939	55
1903	Kelley Joseph Henry Hart	Dorchester	February 18 1940	62
1880	Kuttredge, Joseph	North Andover	January 31 1940	81
1894	†Lamoureux Joseph Elzear	Lowell	March 16, 1940	71
1900	Lane, Walter Appleton	Milton	January 21, 1940	67
1897	Leary William Charles	Springfield	October 13 1939	70
1900	Legg Arthur Thornton	Providence, R. I	July 8 1939	65
1935	Lobo Joseph Paulo	Boston	November 28 1939	62
1896	Lord Sidney Archer	Brighton	March 30 1940	71
1920	Loring Benjamin Tappan	Watertown	July 29 1939	70
1900	†Lovell Martha Eleanor	Boston	April 22 1940	Unknown
1913	Luce, LeRoy Alson	Boston	September 27 1939	60
1899	Mains Charles Frederick	Dorchester	August 17 1939	67
1915	Mains Herbert Llewellyn	Danvers	April 6 1940	62
1903	Marshall, Augustus Thompson	Randolph Vt.	Unknown	64
1915	Mathewson Frank Weedon	New Bedford	July 6, 1939	48
1908	McIntire, George Francis	West Barrington R. I	January 9 1940	69
1892	Mead George Nathaniel Plummer	Winchester	December 14 1939	80
1904	Moline, Charles	Sunderland	November 15 1939	63
1890	Morse, John Lovett	Newton	April 3 1940	75
1884	†Munro Walter Lee	Providence, R. I	October 23 1939	82
1895	Noble, Angenette Fowler	Westfield	April 30 1940	79
1903	Nye, Harry Royal	Leominster	January 8 1940	68
1906 } 1916 }	Oak, Charles Arthur	Lynn	November 15 1939	60
1902	O'Brien Walter John Leo	Jamaica Plain	May 1 1940	66
1930	Page, Pearson Sterling	Andover	May 23 1939	67
1891	†Payne, James Henry	Allston	January 31 1940	77
1916 } 1921 }	Peck, Martin William	Boston	May 7 1940	60
1899	Perce, George Alphonso	Lowell	February 21 1940	65
1904 } 1928 }	Pope, Ernest Folger	Boston	January 26, 1940	65



1908	Pratt, David Damon	New Bedford	January 29, 1940	59
1910	Preble, William Emerson	Boston	January 22, 1940	64
1896	Rice, Walter Henry	Boston	April 19, 1940	68
1911	Riggs, Austen Fox	Stockbridge	March 5, 1940	64
1929	Roberts, Sumner Mead	Hyannis	November 19, 1939	41
1912	Salles, John Murray	New Bedford	November 26, 1939	55
1905	Scanlan, Thomas John	West Roxbury	October 18, 1939	67
1906	†Schmidt, Richard Deidrich	Dorchester	December 18, 1939	68
1884	†Sparhawk, Clement Willis	Salem	October 22, 1939	85
1891	Sules, Fred Merritt	Waltham	May 10, 1940	76
1932	Stivers, George Lincoln	Tucson, Ariz.	November 26, 1939	62
1914	Thompson, Charles Arthur	Newton	February 3, 1940	67
1870	†Thompson, Frederick Henry	Fitchburg	December 14, 1939	95
1916	Van Gaasbeek, George Henry	Springfield	January 22, 1940	76
1882	†Vickery, Herman Frank	Brookline	February 22, 1940	84
1914	†Wagner, Emma Juliet	West Somerville	June 12, 1939	76
1904	Walcott, Henry Joel	Concord	April 17, 1940	67
1933	Weinger, Morris Aaron	Lynn	January 27, 1940	40
1922	White, Frank Dunster	Milford	August 28, 1939	63
1935	Wilkinson, William D	Boston	September 23, 1939	41
1910	Wright, William Francis	Miami, Fla	April 11, 1940	59
1914	Young, Edward Wallace	New Bedford	April 16, 1940	53

†Retired fellow

Total number of deaths of active fellows	81
Total number of deaths of retired fellows	18
Grand total	99

## OFFICERS FOR 1940-1941

ELECTED BY THE COUNCIL, MAY 21, 1940

PRESIDENT Walter G Plippen, Salem, 31 Chestnut Street.  
 VICE PRESIDENT Frank R Ober, Boston, 234 Marlboro Street.

SECRETARY Alexander S Begg, West Roxbury Office, Boston, 8 Fenway

TREASURER Charles S Butler, Boston, 257 Newbury Street.

ORATOR A Warren Stearns, Billerica Office, Boston, 520 Commonwealth Avenue.

## STANDING COMMITTEES FOR 1940-1941

ELECTED BY THE COUNCIL, MAY 21, 1940

## PUBLICATIONS—Established 1825

## DATE OF APPOINTMENT

F H Lahey	June 6, 1933 (appointed chairman February 7, 1940)
R M Smith	June 6, 1933
J P O'Hare	June 9, 1936
Conrad Wesselhoef	June 2, 1937
W B Breed	February 7, 1940

## ARRANGEMENTS—Established 1849

E. J. O'Brien	June 9, 1936 (appointed chairman May 21, 1940)
W T O'Halloran	June 2 1937
J A Halsted	June 1, 1938
G P Sturgis	June 7, 1939
H H Faxon	May 21, 1940

## ETHICS AND DISCIPLINE—Established 1871

R. L. DeNormandie	June 11, 1929 (appointed chairman June 1, 1938)
R. R. Stratton	June 9, 1936
W J Brickley	February 3, 1937
A G Rice	June 1, 1938
F R. Jouett	May 21, 1940

## MEDICAL EDUCATION AND MEDICAL DIPLOMAS—Established 1881

J P Monks	June 7, 1939 (appointed chairman May 21, 1940)
A W Stearns	June 9, 1936
A R. Gardner	June 1, 1938
G D Henderson	June 1, 1938
L. S. McKittrick	May 21, 1940

## STATE AND NATIONAL LEGISLATION—Established 1894

E L Merritt	May 21, 1940 (chairman)
D L Lionberger	June 4, 1935
B F Conley	June 2, 1937
C A Robinson	June 1, 1938
E. M. Chapman	June 7, 1939

## MEMBERSHIP—Established 1897

G C Caner	June 17, 1930 (appointed chairman May 21, 1940)
J E. Fish	June 17, 1930
H. F. Newton	June 9, 1931
P H Leavitt	June 1, 1938
A W Reggio	May 21, 1940

## PUBLIC HEALTH—Established 1912

F P Denny	June 1, 1938 (appointed chairman June 7, 1939)
Gerald Hoeffel	June 17, 1930

S. C. Dalrymple	June 4 1935
H. L. Lombard	June 4 1935
H. F. Day	June 7, 1939

**MEDICAL DEFENSE** — Established 1927

A. W. Allen	June 7 1927 (appointed chairman June 7 1939)
E. D. Gardner	June 7 1927
F. B. Sweet	June 7 1927
W. R. Morrison	June 9 1936
Horatio Rogers	June 7, 1939

**PERMANENT HOME** — Established 1932.

W. H. Robey	February 24 1937 (chairman)
C. G. Mixer	June 8 1932
J. M. Burne	June 8 1932
C. S. Butler	June 4 1935
E. C. Miller	June 4 1935

**FINANCIAL PLANNING AND BUDGET** — Established 1938

John Homans	June 2 1938 (chairman)
E. L. Hunt	June 2, 1938
C. F. Wilinsky	June 2 1938
E. J. O'Brien	June 2, 1938
P. P. Johnson	October 4 1939

**SPECIAL COMMITTEES FOR 1940 1941****CANCER** — Established 1917

Shields Warren chairman F. G. Balch E. M. Daland  
P. E. Truesdale, C. C. Simmons.

**REPRESENTATIVES TO THE MASSACHUSETTS CENTRAL HEALTH COUNCIL**

Barnstable W. D. Kinney  
Berkshire R. J. Carpenter  
Hampden G. D. Henderson  
Middlesex North M. A. Tighe  
Suffolk R. B. Osgood  
Worcester E. C. Miller

**PUBLIC EDUCATION** (a subcommittee of the Committee on Public Health) — Established 1930

F. P. Denny chairman Gerald Hoeftel secretary  
G. R. Minot, W. H. Robey R. M. Smith E. H. Place,  
C. C. Simmons, J. H. Pratt, H. W. Stevens J. B.  
Ayer H. P. Mosher F. R. Ober E. P. Joslin J. D.  
Barney H. L. Lombard

**PUBLIC RELATIONS** — Established 1931 (One member appointed yearly by each district medical society the president of the Society is chairman.)

BARNSTABLE DISTRICT MEDICAL SOCIETY  
M. E. Champion North Harwich

BERKSHIRE DISTRICT MEDICAL SOCIETY  
P. J. Sullivan, Dalton 471 Main Street.

BRISTOL NORTH DISTRICT MEDICAL SOCIETY  
F. H. Dunbar Mansfield. Office, Boston 43 Bay State Road

BRISTOL SOUTH DISTRICT MEDICAL SOCIETY  
A. J. Pothier New Bedford 720 County Street.

ESSEX NORTH DISTRICT MEDICAL SOCIETY  
E. S. Bagnall Groveland 281 Main Street.

ESSEX SOUTH DISTRICT MEDICAL SOCIETY  
G. A. Fenn, Beverly 19 Abbott Street.

FRANKLIN DISTRICT MEDICAL SOCIETY  
H. G. Stetson Greenfield 39 Federal Street.

HAMPDEN DISTRICT MEDICAL SOCIETY  
P. E. Gear Holyoke, 188 Chestnut Street.

HAMPSHIRE DISTRICT MEDICAL SOCIETY  
E. E. Thomas, Northampton, 59 West Street.

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY  
J. H. Blaisdell Winchester Office, Boston, 45 Bay State Road.

MIDDLESEX NORTH DISTRICT MEDICAL SOCIETY  
M. A. Tighe, Lowell 9 Central Street.

MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY  
D. C. Dow Cambridge, 1587 Massachusetts Avenue.

NORFOLK DISTRICT MEDICAL SOCIETY  
F. P. McCarthy Milton. Office Boston, 371 Commonwealth Avenue.

NORFOLK SOUTH DISTRICT MEDICAL SOCIETY  
W. G. Curtis Wollaston, 10 Grand View Avenue.

PLYMOUTH DISTRICT MEDICAL SOCIETY  
C. D. McCann Brockton 12 Cottage Street.

SUFFOLK DISTRICT MEDICAL SOCIETY  
A. A. Hornor Boston 319 Longwood Avenue.

WORCESTER DISTRICT MEDICAL SOCIETY  
C. A. Sparrow Worcester 73 Sagamore Road

WORCESTER NORTH DISTRICT MEDICAL SOCIETY  
J. J. Curley Leominster, 82 Main Street.

**POSTGRADUATE INSTRUCTION** — Established 1932.

F. R. Ober chairman L. E. Parkins secretary F. D. Adams Roy Morgan J. M. Birnie, H. L. Higgins,  
J. W. O'Connor C. W. Blackett, Jr., R. B. Osgood  
Reginald Fitz, A. S. Begg C. S. Burwell A. W. Stearns W. H. Robey R. N. Nye, H. D. Chadwick,  
C. M. Campbell Lincoln Davis.

**PHYSICAL THERAPY** — Established 1935

F. P. Lowry chairman R. B. Osgood G. R. Minot.

**COMMITTEE TO CONSIDER EXPERT TESTIMONY** — Established 1936

G. L. Schadt, chairman David Cheever, J. J. Goodwin  
F. P. McCarthy H. C. Marble.

**AUTOMOBILE INSURANCE CLAIMS** — Established 1937

H. C. Marble, chairman H. M. Landesman secretary  
P. P. Henson.

**CONVALESCENT CARE** — Established 1938.

T. D. Jones, chairman H. E. Gallup

**INDUSTRIAL HEALTH** — Established 1939

W. I. Clark, chairman N. G. Monroe, L. R. Daniels,  
H. G. Murray T. L. Shipman.

**AREA MEDICAL LIBRARY AND MUSEUM** — Established 1939

H. R. Viets, chairman R. B. Osgood, Benjamin Spector

# COMMITTEE TO STUDY PRACTICE OF MEDICINE BY UNREGISTERED PERSONS—Established 1939

Richard Dutton, chairman, B F Conley, E F Timmons

# TWENTY FIVE VOTING MEMBERS IN THE ASSOCIATED HOSPITAL SERVICE CORPORATION—Established 1939

B H Alton, E S Bagnall, G M Balboni, W B Breed, L D Chapin, H F Day, J F Donaldson, A W Dudley, J M Fallon, J E Flynn, A R Gardner, H W Godfrey, D C Halbersleben, J A Halsted, J H Lambert, A A Levi, A E Parkhurst, Helen S Pitman, A G Rice, A T Ronan, F W Snow, G L Steele, R P Stetson, J E Talbot, E. L. Young

# COMMITTEE TO STUDY PROPOSALS FOR BUDGETING MEDICAL CARE—Established 1940

T H Lanman, chairman, J M Birnie, J C McCann, M A Tighe, Shields Warren

# DELEGATES AND ALTERNATES TO THE HOUSE OF DELEGATES, AMERICAN MEDICAL ASSOCIATION FOR 1940-1941

## DELEGATES

## ALTERNATES

June 1, 1939 to June 1, 1941

E F Cody, New Bedford	E L. Merritt, Fall River
J M Birnie, Springfield	R J Carpenter, North Adams
R H Miller, Boston	Cadis Phipps, Brookline

June 1, 1940 to June 1, 1942

D D Scannell, Jamaica Plain	E. S. Bagnall, Groveland
Dwight O Hara, Waltham	E. L. Hunt, Worcester
C E. Mongan, Somerville	M A Tighe, Lowell
W G Pluppen, Salem	J I B Vail, Hyannis

# COUNCILORS FOR 1940-1941

ELECTED BY THE DISTRICT MEDICAL SOCIETIES AT THEIR ANNUAL MEETINGS, APRIL 15 TO MAY 15, 1940

## BARNSTABLE

O S Simpson, Falmouth, 59 Locust St, V P  
M E Champion, North Harwich, A M N C  
D E Higgins, Cotuit, Main St, Sec.  
W D Kinney, Osterville, M. N C  
E S Osborne, West Dennis

## BERKSHIRE

J W Bunce, North Adams, 85 Main St, V P  
J J Boland, Pittsfield, 334 North St.  
V P Cummings, North Adams, 57 Main St.  
I S F Dodd, Pittsfield, 34 Fenn St.  
H J Downey, Pittsfield, 184 North St, M N C  
C. F. Frisce, Pittsfield, 311 North St, A M N C.  
C. F. Kernan, Pittsfield, 184 North St.  
G S Reynolds, Pittsfield, 7 North St, Sec.  
P J Sullivan, Dalton, 471 Main St.

## BRISTOL NORTH

R. M. Chambers, Taunton, Taunton State Hospital, V P

W H Allen, Mansfield, 70 North Main St, M N C.  
F H Dunbar, Mansfield, Office Boston, 43 Bay State Rd, A M N C  
F V Murphy, Attleboro, 79 Bank St.  
J L. Murphy, Taunton, 23 Cedar St.  
W H Swift, Taunton, 141 High St, Sec.

## BRISTOL SOUTH

H E Perry, New Bedford, 159 Cottage St, V P  
G W Blood, Fall River, 82 New Boston Rd.  
R. B. Butler, Fall River, 278 North Main St, A M N C  
E. F. Cody, New Bedford, 105 South Sixth St, M N C  
J A Fournier, Fall River, 11 Choate St.  
E. D. Gardner, New Bedford, 150 Cottage St.  
F M. Howes, New Bedford, 135 Cottage St.  
E L. Merritt, Fall River, 130 Rock St, C  
D R. Mills, Edgartown  
A. H. Sterns, New Bedford, 31 Seventh St, Sec.  
I N Tilden, Mattapoisett, Barstow St.  
C C Tripp, New Bedford, 416 County St.  
P E Truesdale, Fall River, 151 Rock St.

## ESSEX NORTH

R C Norris, Methuen, 247 Broadway, V P  
E. S. Bagnall, Groveland, 281 Main St, A M N C  
R V Baketel, Methuen, 7 Hampshire St.  
C S Benson, Haverhill, 30 Summer St.  
E. H. Ganley, Methuen, 251 Broadway  
H. R. Kurth, Lawrence, 477 Essex St, Sec.  
P J Look, Andover, 115 Main St.  
L. C. Pearce, Newburyport, 279 High St.  
G L. Richardson, Haverhill, 94 Emerson St.  
F W Snow, Newburyport, 24 Essex St, M. N C  
T N Stone, Haverhill, 3 Washington Sq  
C F Warren, Amesbury, 1 School St.  
C A. Weiss, Lawrence, 160 Jackson St.

## ESSEX SOUTH

Loring Grimes, Swampscott, 84 Humphrey St, V P  
H A Boyle, Middleton, Essex County Tuberculosis Sanatorium  
N P Breed, Lynn, 9 Washington Sq  
C L. Curtis, Salem, 101 Federal St.  
J F Donaldson, Salem, 32 Lynde St.  
R. E. Foss, Peabody, 125 Main St.  
S E Golden, Beverly, 38 Ocean St.  
R P Hallett, Gloucester, 63 Middle St.  
P P Johnson, Beverly, 1 Monument Sq  
J F Jordan, Peabody, 76 Lynn St, A. M N C  
B B Mansfield, Ipswich, 4 Green St.  
A E. Parkhurst, Beverly, Monument Sq  
W G Pluppen, Salem, 31 Chestnut St, President.  
Horace Poirier, Salem, 197 Lafayette St, M. N C  
E. D. Reynolds, Danvers, 48 High St.  
J R. Shaughnessy, Salem, 24½ Winter St, Sec.  
R E Stone, North Beverly, 15 Lakeview Ave.  
J W Trask, East Lynn, 90 Ocean St.  
C F Twomey, East Lynn, 80 Ocean St.

## FRANKLIN

A H Wright, Northfield, 111 Main St, V P  
F J Barnard, Greenfield, 479 Main St, M N C  
H L Craft, Ashfield, Sec.  
A H. Ellis, Greenfield, 58 Federal St.  
W J Pelletier, Turners Falls, 171 Ave. A, A M N C  
H G Stetson, Greenfield, 39 Federal St, Ex Pres

## HAMPTDEN

J. B. Bigelow Holyoke, 109 Suffolk St., V P  
 P. H. Allen Holyoke, 16 Fairfield Ave.  
 T. S. Bacon Springfield, 69 Maple St.  
 E. P. Bagg Holyoke, 207 Elm St.  
 W. C. Barnes Springfield, 146 Chestnut St., Sec.  
 J. M. Birnie Springfield, 146 Chestnut St., Ex. Pres.  
 W. A. R. Chapin Springfield, 121 Chestnut St.  
 J. L. Chereskin, Springfield, 333 Bridge St.  
 A. J. Douglas, Westfield 93 Elm St.  
 E. C. Dubois Springfield 174 Buckingham St.  
 G. L. Gabler Holyoke, 98 Suffolk St.  
 M. F. Gaynor Springfield 44 Chestnut St.  
 P. E. Gear Holyoke, 188 Chestnut St.  
 Frederic Hagler Springfield, 20 Maple St.  
 G. D. Henderson, Holyoke, 312 Maple St.  
 E. A. Knowlton, Holyoke, 207 Elm St.  
 M. W. Pearson Ware, 19 Pleasant St.  
 A. G. Rice Springfield 33 School St.  
 G. L. Schadt, Springfield 44 Chestnut St., M. N. C.  
 G. L. Steele, Springfield, 20 Maple St., A. M. N. C.

## HAMPSHIRE

J. M. Murphy Florence, 91 North Main St., V P  
 A. J. Bonnevill, Hatfield, 60 Main St.  
 J. D. Collins, Northampton, 187 Main St., Sec.  
 L. N. Durgin, Amherst, 66 Amity St., M. N. C.  
 L. B. Pond, Easthampton, 115 Main St., A. M. N. C.  
 E. E. Thomas, Northampton 59 West St.

## MIDDLESEX EAST

G. R. Murphy Melrose, 244 Main St., V P  
 C. R. Bauley Reading 46 Woburn St.  
 J. H. Blaisdell, Winchester Office Boston 45 Bay State Rd., A. M. N. C.  
 Richard Dutton, Wakefield 33 Avon St.  
 E. M. Halligan Reading 37 Salem St.  
 J. H. Kerrigan, Stoneham, 481 Main St.  
 K. L. MacLachlan, Melrose, 1 Bellevue Ave., Sec.  
 R. W. Sheehy Winchester 21 Washington St.  
 R. R. Stratton, Melrose, 538 Lynn Fells Parkway  
 M. N. C.

## MIDDLESEX NORTH

W. M. Collins Lowell, 174 Central St., V P  
 M. L. Alling Lowell, 9 Central St.  
 R. L. Drapeau, Lowell 310 Merrimack St., Sec.  
 D. J. Ellison, Lowell, 8 Merrimack St.  
 F. L. Gage, Lowell, 9 Central St. M. N. C.  
 A. R. Gardner Lowell 16 Shattuck St.  
 G. A. Leahy Lowell 128 Merrimack St.  
 E. O. Tabor Lowell 16 Shattuck St.  
 M. A. Tighe, Lowell, 9 Central St., A. M. N. C.

## MIDDLESEX SOUTH

Dwight O'Hara, Waltham Office Boston, 5 Bay State Rd., V P  
 C. F. Atwood, Arlington 821 Massachusetts Ave.  
 E. W. Barron, Malden Office Boston, 20 Ash St.  
 W. B. Bartlett, Concord, 28 Monument St.  
 Harris Bass, Everett, 351 Broadway  
 E. H. Bigelow Framingham Center 31 Pleasant St., Ex. Pres.  
 G. F. H. Bowers, Newton Highlands, 156 Woodward St.  
 R. W. Buck, Waban, Office Boston, 5 Bay State Rd.  
 E. J. Butler Cambridge, 25 Garden St.  
 Richard Collins, Jr., Waltham, 826 Main St.

B. F. Conley Malden 51 Main St.  
 P. A. Consales, Belmont, Office Boston, 481 Beacon St.  
 D. F. Cummings, Natick, 12 East Central St.  
 C. H. Dalton, Somerville, 440 Broadway  
 H. F. Day Cambridge, Office Boston 412 Beacon St.  
 C. L. Derick Newton Highlands, Office Boston 412 Beacon St.  
 J. E. Dodd, Framingham 259 Union Ave.  
 A. W. Dudley Cambridge, 1740 Massachusetts Ave., M. N. C.  
 E. R. Fleming Medford 322 Boston Ave.  
 \*H. Q. Gallupe, Waltham, 751 Main St.  
 F. W. Gage Malden 105 Salem St.  
 H. G. Giddings, Newton Centre, Office Boston 270 Commonwealth Ave.  
 H. W. Godfrey Auburndale, 14 Hancock St.  
 B. I. Goldberg Newton Centre, Office Boston 481 Beacon St.  
 W. G. Grandison Charlestown 65 High St.  
 A. D. Guthrie, Medford, 408 Salem St.  
 A. M. Jackson, Everett, 512 Broadway  
 A. A. Levi Newton, Office Boston, 481 Beacon St., Sec.  
 F. P. Lowry Newton 313 Washington St.  
 A. N. Makechue, Cambridge, 14 Upland Rd.  
 R. A. McCarty Waltham 751 Main St.  
 J. A. McLean West Somerville, 16 Curtis St.  
 Edward Mellus Newton 15 Clements Rd.  
 J. C. Merriam, Framingham 198 Union Ave.  
 C. E. Morgan Somerville, 24 Central St., Ex. Pres.  
 J. P. Nelligan, Cambridge, 2336 Massachusetts Ave.  
 E. J. O'Brien, Brighton, Office Boston, 270 Commonwealth Ave. C.  
 L. S. Pilcher Newton Centre, 43 Parker St.  
 Max Ruvio Newton, Office Boston, 485 Commonwealth Ave.  
 E. S. A. Robinson Newton Centre Office Jamaica Plain 375 South St.  
 E. F. Ryan Maynard, 74 Main St.  
 E. J. Sawyer Newton, 488 Centre St.  
 M. J. Schlesinger Newton Office Boston, 330 Brookline Ave.  
 W. N. Secord, Watertown 128 Mt. Auburn St.  
 J. W. Sever Cambridge, Office Boston, 321 Dartmouth St.  
 E. F. Sewall Somerville, 380 Broadway  
 E. W. Small Belmont, 68 Leonard St.  
 H. P. Stevens, Cambridge, 1 Craigie St.  
 R. A. Taylor Waltham, 550 Moody St.  
 H. W. Thayer Newtonville, 355 Walnut St.  
 J. H. Townsend Belmont, Office Boston, 319 Longwood Ave.  
 Fresenius Van Nuy West 338 Boston Post Rd.  
 A. M. N. C.  
 R. H. Wells, Lexington 1430 Massachusetts Ave.  
 M. W. White, Somerville, 21 Walnut St.  
 W. S. Whittemore, Cambridge, 3 Concord Ave.  
 Alfred Worcester Waltham, 314 Bacon St., Ex. Pres.  
 Hovhannes Zovickian, Watertown 528 Mt. Auburn St.

## NORFOLK

F. P. McCarthy Milton, Office Boston 371 Commonwealth Ave., V P  
 J. D. Adams, Brookline, Office Boston, 43 Bay State Rd.  
 F. J. Bailey Dorchester, 40 Hancock St.  
 J. R. Barry West Roxbury 1857 Center St.  
 Carl Bearse, Boston, 483 Beacon St.

A S Begg, West Roxbury, Office Boston, 8 Fenway, Secretary  
 M I Berman, Dorchester, 1071A Blue Hill Ave.  
 G F Blood, Roslindale, 20 Belgrade Ave.  
 F S Cruickshank, Brookline, 1247 Beacon St., Sec.  
 William Dameshek, Brookline, Office Boston, 371 Commonwealth Ave.  
 F P Denny, Brookline, 111 High St., C  
 G L Doherty, West Roxbury, Office Boston, 466 Commonwealth Ave.  
 D G Eldridge, Dorchester, 15 Monadnock St.  
 J J Elliott, Roslindale, 4258 Washington St.  
 H M Emmons, Needham, Office Boston, 354 Commonwealth Ave.  
 J C V Fisher, West Roxbury, Office Boston, 510 Commonwealth Ave.  
 Susannah Friedman, Roxbury, Office Boston, 485 Commonwealth Ave.  
 Maurice Gerstein, Brookline, 1894 Beacon St.  
 David Glunts, Roxbury, 2 Franklin Garden  
 W A Griffin, Sharon, Office Boston, 311 Beacon St.  
 B T Guild, Dorchester, Office Boston, 475 Commonwealth Ave.  
 J B Hall, Roxbury, 60 Windsor St.  
 R. J. Heffernan, Jamaica Plain, Office Brookline, 1101 Beacon St.  
 Morris Ingall, Roxbury, Office Boston, 485 Commonwealth Ave.  
 H J Inglis, Chestnut Hill, Office Boston, 43 Bay State Rd., A M N C  
 I R Jinkelson, Jamaica Plain, Office Boston, 483 Beacon St.  
 H L Johnson, West Roxbury, Office Boston, 520 Commonwealth Ave.  
 C J Kickham, Brookline, Office Boston, 524 Commonwealth Ave.  
 C J L. Kickham, Jamaica Plain, Office Boston, 12 Bay State Rd.  
 E. L. Kickham, Brookline, Office Boston, 270 Commonwealth Ave.  
 D L. Lionberger, Dedham, Office Roslindale, 3 Conway St.  
 D S Luce, Canton, 553 Washington St.  
 D L. Lynch, Roslindale, Office Boston, 245 State St.  
 T F P Lyons, Milton, Office Boston, 270 Commonwealth Ave.  
 Charles Malone, Jamaica Plain, 46 St. John St.  
 F J Moran, Dedham, 395 Washington St.  
 M W O'Connell, West Roxbury, Office Boston, Boston City Hospital  
 Frederick Reis, Jamaica Plain, Office Boston, 416 Huntington Ave.  
 S A Robins, Roxbury, Office Boston, 636 Beacon St.  
 S M Saltz, Roxbury, 294 Seaver St.  
 D D Scannell, Jamaica Plain, Office Boston, 475 Commonwealth Ave., M N C  
 Nathan Sidel, Brookline, Office Boston, 483 Beacon St.  
 J W Spellman, Milton, Office Brookline, 1101 Beacon St.  
 M H Spellman, Jamaica Plain, Office Boston, 475 Commonwealth Ave.  
 J P Treanor, Jr., Jamaica Plain, Office Brookline, 1101 Beacon St.  
 W J Walton, Dorchester, 106 Bowdoin St.  
 H F R. Waits, Dorchester, 6 Monadnock St.  
 N A Welch, West Roxbury, Office Boston, 520 Commonwealth Ave.

## NORFOLK SOUTH

D B Reardon, Quincy, 1186 Hancock St., V P  
 C. S. Adams, Wollaston, 62 Brook St.  
 H H A Blyth, Quincy, 24 Russell Park, Sec.  
 R. L. Cook, Quincy, 38 Russell Park.  
 W G Curtis, Wollaston, 10 Grand View Ave., M N C  
 G E Emerson, South Weymouth, 52 Columbia St.  
 G V Higgins, Randolph, 190 North Main St., A. M. N C  
 H A Robinson, Hingham, North St.  
 W L. Sargent, Quincy, 24 Whitney Rd.  
 Charles Whelan, Cohasset, Office Boston, 395 Commonwealth Ave.

## PLYMOUTH

S W Goddard, Brockton, 129 West Elm St., V P  
 J E Brady, Brockton, 231 Main St.  
 A L Duncombe, Brockton, 167 Newbury St.  
 P B Kelly, Plymouth, 27 Court St.  
 P H Leavitt, Brockton, 129 West Elm St., A M N C  
 R. C. McLeod, Brockton, 129 West Elm St., Sec.  
 G A Moore, Brockton, 167 Newbury St.  
 D W Pope, Brockton, 12 Cottage St.  
 W H Pulsifer, Whitman, 26 Park Ave., M N C  
 F F Weiner, Brockton, 231 Main St.

## SUFFOLK

A A Hornor, Boston, 319 Longwood Ave., V P  
 A W Allen, Boston, 264 Beacon St., C  
 J W Bartol, Boston, 1 Chestnut St., Ex-Pres  
 W B Breed, Boston, 264 Beacon St., M N C  
 W J Brickley, Boston, 274 Boylston St.  
 W E Browne, Boston, 587 Beacon St.  
 C S Butler, Boston, 257 Newbury St., Treasurer  
 G C Caner, Boston, 63 Marlboro St., C  
 E M Chapman, Boston, 270 Commonwealth Ave.  
 David Cheever, Boston, 193 Marlboro St.  
 M H. Clifford, Boston, 270 Commonwealth Ave., Sec.  
 H M Clute, Boston, 171 Bay State Rd.  
 Lincoln Davis, Boston, 279 Beacon St.  
 R. L. DeNormandie, Boston, 330 Dartmouth St., A. M. N C, C  
 N W Faxon, Boston, Massachusetts General Hospital.  
 G B Fenwick, Chelsea, 38 Cary Ave.  
 \*Reginald Fitz, Boston, 319 Longwood Ave.  
 Channing Frothingham, Boston, Office Jamaica Plain, 1153 Centre St., Ex Pres  
 M N Fulton, Boston, 721 Huntington Ave.  
 Joseph Garland, Boston, 264 Beacon St.  
 John Homans, Boston, 721 Huntington Ave., C  
 Rudolph Jacoby, Boston, 270 Commonwealth Ave.  
 E P Joshn, Boston, 81 Bay State Rd.  
 H A. Kelly, Winthrop, 200 Pleasant St.  
 F H Lahey, Boston, 605 Commonwealth Ave., C  
 T H Lanman, Boston, 300 Longwood Ave.  
 R I Lee, Boston, 264 Beacon St.  
 C C Lund, Boston, 319 Longwood Ave.  
 G R Minot, Boston, Boston City Hospital  
 W J Mixer, Boston, 319 Longwood Ave.  
 J P Monks, Boston, 330 Dartmouth St., C  
 Donald Munro, Boston, 818 Harrison Ave.  
 H L Musgrave, Revere, 622 Beach St.  
 R N Nye, Boston, 8 Fenway  
 F R Ober, Boston, 234 Marlboro St., Vice-Pres  
 J P O'Hare, Boston, 520 Commonwealth Ave.  
 L E Parkins, Boston, 12 Bay State Rd.

Interim appointment

L. E. Phaneuf, Boston 270 Commonwealth Ave.  
 Helen S. Pittman, Boston 412 Beacon St.  
 W. H. Robey Boston 202 Commonwealth Ave., Ex  
 Pres., C.  
 G. C. Shattuck, Boston 25 Shattuck St.  
 R. M. Smith Boston 66 Commonwealth Ave.  
 M. C. Sosman, Boston, 721 Huntington Ave.  
 Augustus Thorndike, Jr., Boston, 319 Longwood  
 Ave., C.  
 E. F. Timmins South Boston 527 Broadway  
 S. N. Vose, Boston 29 Bay State Rd.  
 Shields Warren, Boston 195 Pilgrim Rd.  
 Conrad Wesselhoef, Boston 315 Marlboro St.  
 C. F. Wilinsky Boston, 330 Brookline Ave.

#### WORCESTER

J. M. Melick, Worcester 27 Elm St., V P  
 J. C. Austin, Spencer 176 Main St.  
 Gordon Berry Worcester 36 Pleasant St.  
 W. P. Bowers, Clinton, 264 Chestnut St. Ex Pres.  
 L. R. Bragg Webster 260 Main St.  
 P. H. Cook, Worcester 27 Elm St.  
 W. J. Delahanty Worcester 5 Trumbull Sq  
 G. A. Dix, Worcester 6 Ashland St.  
 E. B. Emerson, Rutland Rutland State Sanatorium.  
 G. E. Emery Worcester 340 Main St.  
 J. M. Fallon Worcester 390 Main St.  
 J. J. Goodwin Clinton, 199 Chestnut St.  
 E. L. Hunt, Worcester 28 Pleasant St.  
 E. R. Leib Worcester 36 Pleasant St.  
 W. F. Lynch Worcester 390 Main St., A. M. N. C.  
 A. W. Marsh Worcester 690 Main St.  
 J. C. McCann, Worcester, 390 Main St.  
 J. W. O'Connor Worcester 36 Pleasant St.  
 W. C. Seelye, Worcester 390 Main St.  
 C. A. Sparrow Worcester 21 West St.  
 G. C. Tully Worcester 390 Main St., Sec.  
 R. J. Ward, Worcester 9 Bellevue St.  
 F. H. Washburn, Holden, Holden Clinic.  
 R. P. Watkins Worcester 332 Main St., M. N. C.  
 S. B. Woodward, Worcester 58 Pearl St., Ex Pres.

#### WORCESTER NORTH

B. P. Sweeney Leominster 5 Gardner Place, V P  
 E. A. Adams, Fitchburg 40 Oliver St., Sec.  
 H. C. Arey Gardner 66 Parker St., A. M. N. C.  
 J. J. Curley Leominster 82 Main St.  
 T. R. Donovan Fitchburg 42 Fox St.  
 C. B. Gay Fitchburg 62 Day St., M. N. C.  
 J. C. Hales, Gardner 66 Parker St.

The initials M. N. C. following the name of an officer indicate that he is a member of the Nominating Committee and the initials M. M. S. indicate that he is an alternate member of the Nominating Committee. V. P. indicates that the member is an officer by virtue of his office as president of a district society and so vice-president of the general society. C. indicates that he is chairman of a standing committee. Sec. that he is secretary of his district society and Ex Pres. that he is an officer by virtue of being a past president.

#### CENSORS FOR 1940-1941

##### BARNSTABLE

W. D. Kinney Osterville, supervisor  
 C. E. Harris, Hyannis.  
 J. P. Nickerson West Harwich.  
 J. H. Higgins Marston Mills.  
 D. H. Hiebert, Provincetown.

##### BERKSHIRE

J. S. F. Dodd, Pittsfield, supervisor  
 J. F. McLaughlin, Adams  
 John Hughes, Pittsfield.

G. M. Shipton Pittsfield.  
 G. S. Wickham Lee.

#### BRISTOL NORTH

W. H. Allen, Mansfield supervisor  
 W. H. Bennett, Jr., Taunton.  
 L. E. Butler Taunton.  
 C. B. Kingsbury Taunton.  
 H. L. Rich, Attleboro.

#### BRISTOL SOUTH

F. M. Howes New Bedford supervisor  
 W. F. Macknight, Fall River  
 E. A. McCarthy Fall River  
 Henry Wardle, Fall River  
 C. C. Persons New Bedford.

#### ESSEX NORTH

R. V. Baketel Methuen supervisor  
 P. W. Blake, Andover  
 J. P. Creed Haverhill  
 J. F. Curtin Lawrence.  
 W. C. Hardy Haverhill.

#### ESSEX SOUTH

A. E. Parkhurst Beverly supervisor  
 S. R. Davis, Lynn.  
 J. J. Hickey Peabody  
 S. N. Gardner Salem.  
 I. B. Hull Gloucester

#### FRANKLIN

W. J. Pelleener Turners Falls, supervisor  
 A. C. Leach Orange.  
 H. M. Kemp Greenfield.  
 L. R. Dame, Greenfield.  
 K. H. Rice, South Deerfield.

#### HAMPDEN

T. S. Bacon Springfield supervisor  
 E. P. Bagg Holyoke.  
 W. J. Dillon Springfield.  
 G. F. Dalton, Springfield.  
 P. M. Moriarty Chicopee.

#### HAMPSHIRE

A. J. Bonneville, Hatfield, supervisor  
 C. H. Wheeler Haverhill.  
 J. E. Hayes, Northampton.  
 M. E. Cooney Northampton.  
 T. F. Corriden, Northampton.

#### MIDDLESEX EAST

E. M. Halligan Reading supervisor  
 C. E. Montague, Wakefield.  
 J. H. Fay Melrose.  
 M. J. Quinn Winchester  
 N. P. Hersam Stoneham.

#### MIDDLESEX NORTH

M. L. Alling Lowell supervisor  
 J. J. Cassidy Lowell  
 J. Y. Rodger Lowell  
 C. S. Baker Lowell  
 W. F. Ryan Lowell

#### MIDDLESEX SOUTH

J. W. Sever Cambridge, supervisor  
 R. N. Brown Malden  
 H. Q. Gallupe, Waltham  
 C. W. Finnerty West Somerville.  
 J. E. Vance, Natick.

## NORFOLK

B T Guild, Dorchester, supervisor  
J E Fish, Canton  
Hyman Morrison, Roxbury  
O C Leary, Jamaica Plain  
B E Sibley, Brookline

## NORFOLK SOUTH

C S Adams, Wollaston, supervisor  
T B Alexander, Scituate.  
D L Belding, Boston  
J H Cook, Quincy  
C J Lynch, Quincy

## PLYMOUTH

G A Moore, Brockton, supervisor  
J H Dunn, Rockland  
C D McCann, Brockton  
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## REPORT ON MEDICAL PROGRESS

## DIABETES MELLITUS\*

ELLIOTT P. JOSLIN, M.D.†

BOSTON

## TRAUMA AND DIABETES

A RECENT article<sup>1</sup> on traumatic diabetes disturbs me. I fear from reading it that the impression may get abroad that trauma is a not infrequent precursor of diabetes. The authors report two cases which may be summarized as follows:

**CASE 1.** A 26-year-old obese woman, under treatment for several months with injections of Antuitrin-S, whose grand mother was diabetic, was struck by a streetcar on March 4 and thrown to the ground, remaining unconscious for 45 minutes. A life insurance examination had been passed 4 months previously, and repeated examinations of urine the last week before the accident showed it to be sugar-free, as it was immediately after the accident and again on March 6. A spinal puncture yielded 15 cc. of frank blood under normal pressure. The patient was given 1500 units of tetanus antitoxin and 50 cc. of 50 per cent glucose intravenously. On March 8 excessive thirst and frequency of urination began and the fasting blood sugar was 278 mg per 100 cc. This finding was overlooked and the patient was discharged on March 18. The diagnosis was cerebral concussion and multiple lacerations of the scalp.

Subsequently polydipsia, polyuria, a weight loss of 32 pounds, weakness and glycosuria developed. Having shown premonitory symptoms of acidosis for a week, the patient re-entered the hospital April 16 in deep coma, and died 14 hours later.

The medical examiner reported the presence of old, infiltrated blood in the deep layers of the galea. The brain was normal on external examination, and there was no evidence of surface injuries. The vessels at the base of the brain were normal and the ventricles normal in outline and clear, and there was no evidence of injury or disease in the fourth ventricle. The chest and abdominal cavities were normal, and microscopic examination of the organs, including the pancreas, revealed no abnormalities. No mention is made of microscopic examination of the brain.

**CASE 2.** A 14-year-old boy with negative diabetic heredity at the age of 5 years sustained a fractured skull and remained in a hospital for 5 weeks, at the age of 9 he had a second accident, with no definite findings, leaving the hospital in good condition after a few weeks. Tonsillectomy was performed at 10 years, and a physical examination, including the urine, at 12 was normal. During the summer of 1937 an otitis media developed, but cleared up after 2 months. In January, 1938, there was polydipsia, polyuria and a weight loss of 10 pounds, and at the end of 10 days the patient entered the hospital in a semicomatose state. The authors write:

There are no predisposing factors, such as obesity or family history. Whether or not trauma played a part in the obscure etiology we cannot say, but it may be assumed that it did. The case is one of many that we encounter, of sudden onset of diabetes with no demonstrable causative factor, and it emphasizes the importance of further study of such cases.

Lommel<sup>2</sup> reviews and discusses the relation of trauma to diabetes, he inclines to the view that there is no reason to exclude a traumatic etiology merely because one cannot explain such a connection, particularly in the presence of a proved disposition to diabetes.

These two articles have led me to summarize my own views on this question, and some of the reasons for them. But first of all I report two cases which have occurred in my own experience.

**R. T. (No 5786),** a 13-year-old boy, went fishing through the ice on January 2, 1927, and fell in, but was rescued by his setter dog. That night polyuria began, and on January 14 there was 9 per cent of sugar in the urine. On January 26 the urine was sugar-free and the blood sugar was normal, both before and after meals, but the diabetes persisted.

However, I too fell through the ice as a child and my Newfoundland dog played a role in the rescue, yet I did not develop diabetes. Consider the number of boys who yearly have a similar escapade and never contract the disease! In contrast is the following:

The patient (No 13332), a 14-year-old Jewish boy, with diabetic heredity, was in perfect health on December 24, 1934, so far as he or his family knew. That night he slept without rising from bed. On Christmas Day there was no special excitement or careless eating, yet that night he rose six times, and 17 days later, when I first saw him, the urine contained 80 per cent sugar.

There was no accident here to cause diabetes. But suppose he had suffered an injury on Christmas morning—consider the inferences which might have been drawn!

So far as I can remember, no definite case in which I considered trauma a cause of diabetes has occurred among the approximately 19,000 patients with diabetes mellitus and glycosuria who have consulted me. I know of no surgeon who has postponed an operation on a patient because of the possibility that trauma would bring on diabetes. I know of no case in which diabetes has been con-

\*Prepared with the assistance of Howard F. Root, M.D., and Alexander Marble, M.D.

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sidered caused by cerebral shock, embolism or thrombosis. I know of no case in which diabetes has been caused by accidents in the course of college athletics, particularly football, and to fortify my opinion I have recently consulted Dr Arlie V. Bock, of the Department of Hygiene of Harvard University. He<sup>4</sup> writes

So far as I can determine, no case of diabetes following trauma has occurred among athletes at Harvard. We have had many types of injury but no known injury of the pancreas, and whether such trauma might result in diabetes I do not know. You know there has been close medical supervision of athletes at Harvard for at least twenty-five years.

I know of no case in which Dr Harvey Cushing reported diabetes following the development of a tumor in the brain, save those cases in which diabetes occurred in connection with acromegaly and basophilism and 2 cases out of over 200 with chromophobe adenoma. "What is very significant," according to Dr Louise Eisenhardt,<sup>5</sup> "is that in Dr Cushing's own long experience in operating for tumors of the hypophysis or third ventricle he found that such operations did not result in even a transient glycosuria."

Dr Gilbert Horrax<sup>6</sup> writes

I can certainly confirm what Dr Eisenhardt has told you regarding pituitary cases, both from my experience with Dr Cushing's patients and from that with my own. Furthermore, I have been unable to find in my own records any instances of glycosuria in cases with tumors of the fourth ventricle or fourth-ventricle region. However, this much must be said regarding our present cases, that it would be perhaps impossible to tell definitely about a traumatic glycosuria from operation in this region, since we now start all these patients with intravenous glucose at the beginning of the operation, and then if necessary they can have a transfusion without any interruption of the flow of fluid. However before this operative technic I know of no case in our series.

During the World War injuries constantly occurred on the battlefield, but German, French and American writers agreed that they did not result in diabetes.

We have on record in this office the signed statement of a medical observer of pugilistic contests, as follows:

In my twenty-five years of experience in examining boys and men for both amateur and professional boxing throughout the United States, I have never come across one person who has ever had any symptoms or any knowledge on his part submitted to me by him that he had diabetes or had been suffering from diabetes. In all the injuries due to trauma I have never known one injury resulting from trauma that would in any way cause diabetes in any form or any symptoms which would pertain to that disease. During my years of experience, 90 per cent of the people who have participated in boxing exhibitions either in the amateur or professional ranks have had repeated examinations,

and none have ever shown any signs or symptoms of diabetes in any of its forms.

In the article by Geiger and Benson<sup>1</sup> I am mentioned as follows:

Joslin dismisses the question briefly admitting that trauma may aggravate diabetes, but denying a causal relationship. He would discard reports in the older literature because of insufficient proof of previous non-existence of diabetes. He quotes von Noorden's very denusive statement based on the experiences of the World War which he says once and for all bury the question.

In the sixth edition of my book,<sup>6</sup> eight pages were devoted to the question of trauma and diabetes, and forty-four pages were given over to the same topic, with a critical review of the literature and sixty-one references, in the section written by me in *Trauma and Disease*.<sup>7</sup> Since my report there has appeared a volume entitled *Studies of Trauma and Carbohydrate Metabolism with Special Reference to the Existence of Traumatic Diabetes* by Thomsen.<sup>8</sup> The conclusions reached by Thomsen in this monograph are decidedly against trauma as a cause of the disease. An abstract of this volume appeared as an editorial<sup>9</sup> in the *Journal of the American Medical Association*.

The recent work of Young,<sup>10</sup> based on that of Housay Evans and others, in which the injection of anterior pituitary extracts leads to diabetes in animals ultimately resulted in showing that this leads to degeneration of the islands of Langerhans, thus preserving the unity of the diabetes.

It is true that 1 case of possible traumatic diabetes has come to my attention in addition to the 2 cited in my monograph.<sup>6</sup> This case was published by Stern.<sup>11</sup> These 3 cases in which the evidence supports a traumatic origin of diabetes are not absolutely convincing. They are based on the destruction of a large portion of the pancreas, the only cause for diabetes recognized by most observers. As a rule, when injury to the pancreas, theoretically sufficient in extent to cause diabetes, has occurred death has been immediate.

In Stern's case the patient was hit in the left side and back by an automobile on August 12, 1926, suffered with severe pain in the abdomen for 6 days, and when about to leave the hospital on the eighth day went into severe shock and collapsed with agonizing pain in the abdomen. Laparotomy revealed a hemorrhagic pancreatitis with diffuse peritonitis and fat necrosis. Recovery occurred after a 10 months stay in the hospital during which time two large intra-abdominal abscesses were opened. Later a sub-phrenic abscess developed, which was drained. On August 21 the blood sugar was 0.128 mg. per 100 cc. on August 24 0.140 and on August 27 0.160 mg. About November 1929 severe diabetes developed, with a blood sugar of 308 mg. per 100 cc. and 4 per cent sugar in the urine, both of which with dieting returned to normal. The father of the patient had died of diabetes at the age of 84 years; a daughter at the age of 30 had melituria believed to be due to fructose, but the other three children

were apparently free of diabetes Insulin has been taken since March, 1930

Is it surprising that with some 660,000 diabetic patients now alive in this country,<sup>12</sup> and approximately 2,400,000 other individuals in our midst whom we can confidently expect to come down with it before they die, one may discover glycosuria and even diabetes occasionally following the million, more or less, injuries annually which these pre-diabetic people undergo?

#### THE EXPERIMENTAL PRODUCTION OF DIABETES, ITS PREVENTION AND CURE

In contrast to recent skeptical views regarding the preventability of diabetes and its more severe stages, like a fresh breeze comes the news of recent experiments by Best<sup>13</sup> and Lukens<sup>14</sup> indicating clearly the possibility in animals of preventing and even of curing diabetes, a view first enunciated by Naunyn<sup>15</sup> and later confirmed in Allen's laboratory by Copp and Barclay<sup>16</sup> The method of Young,<sup>10</sup> who produced permanent diabetes in dogs by the injection of large amounts of anterior-pituitary extract obtained from bees, has been employed in various laboratories and the resulting experimental conditions carefully studied Campbell, Keenan and Best<sup>17</sup> showed that in such animals the pancreas was almost devoid of insulin and the islets were the seat of hydropic degeneration and atrophy In the spring of 1940 Best<sup>13</sup> announced that if, at the same time that the injection of anterior-pituitary extract was given to the dog, injections of large amounts of insulin were administered, the diabetes failed to appear and that no destructive changes occurred in the islands of Langerhans This was the first demonstration of a means of preventing diabetes by experimental methods Its clinical application lies in the desirability and indication for prompt and aggressive treatment of the disease at the earliest possible moment, as Naunyn<sup>15</sup> stated

Marked differences in the susceptibility to the development of diabetes after injection of anterior-pituitary extract have been known Thus, cats and rats are extremely resistant to its effect, but if a part of the pancreas is first removed the injection of anterior-pituitary extract will lead to diabetes The rat reacts with hypertrophy of the island cells, the cat at first with hydropic degeneration Lukens,<sup>14</sup> using cats, was able to show various stages in the production of diabetes and its cure Thus in the cat with part of the pancreas removed, injections of anterior-pituitary extract were employed using the intraperitoneal route. Large amounts of the extract are required, owing in part to the fact that the inflammatory reaction within the peritoneum undoubtedly destroys a considerable

amount of the active substance injected In the cat the degenerative changes in the islands of Langerhans are gradual in their development They consist of hydropic degeneration, followed after some months by atrophy and disappearance of many of the islands By the end of six months the cats are permanently diabetic On the other hand, during the early months of the diabetogenic injections a section of the pancreas may be removed by surgical means and the hydropic degeneration clearly demonstrated After the cessation of the injections and the development of permanent diabetes of one to four months' duration, if doses of insulin are given in sufficient amounts a later histological examination of the pancreas will show disappearance of the hydropic degeneration, the return of the island cells to normal and, thus, the cure of the diabetes

The possibility of regeneration of the islands of Langerhans when hydropic degeneration has occurred seems to rest on the removal of excessive metabolic strain Apparently the effect of the injection of large amounts of anterior-pituitary substance is exerted in the tissues generally, consisting of increased breakdown of glycogen and an increased formation of glucose from protein This seems to demand an increasing production of insulin by the islands of Langerhans until, by overstrain, degenerative changes are produced Lukens points to cases described by Copp and Barclay,<sup>16</sup> working with Allen years ago, in which, after removal of a portion of the pancreas, hydropic degeneration in the islands was observed In certain animals, by means of proper dietary treatment or by injection of insulin they were able to observe disappearance of the hydropic degeneration Thus, either by diet or by the use of insulin, the islands of Langerhans may be spared and recovery result

The possible clinical significance of these discoveries is immeasurable Some of the peculiarities of acromegalic diabetes seem clearly explained Thus, that only a small percentage of acromegalic patients develop diabetes has its counterpart in the fact that there is observed not only a species difference but a great individual variation in susceptibility of animals to the effect of the injection of anterior-pituitary extract The apparent disappearance of diabetes during certain stages of acromegaly seems to be due to the subsidence of an acute active period of hyperpituitarism, which lasts only long enough to produce hydropic degeneration and then ceases, allowing for regeneration of the islands This also would explain the fact that in the pancreas of some acromegalic patients at autopsy no change is observed in the islands The

question of insulin resistance in acromegaly has been a matter of difference of opinion. Clearly all degrees of severity of diabetes may be expected in different types and stages of acromegaly. Cases requiring as much as 360 units of insulin a day such as that of Ulrich,<sup>16</sup> may within a few days or weeks become so mild as to require no insulin. Yet cases of diabetes long established, as in the cases described by Coggeshall and Root<sup>17</sup> show the usual types of diabetes. In such cases the hypoglycemic effects of insulin are identical with those seen in most diabetic patients.

Shall all cases of extreme insulin resistance be regarded as possible examples of the hypersecretion of some diabetogenic substance from the anterior pituitary gland? In one recent case a young clergyman (Case 17162) during the course of a few months developed such a resistance to insulin that he required 2000 units to recover from coma, and thereafter required a daily dose of 700 to 1500 units. However at the end of eight months his requirement had fallen to 100 units daily. In this case the most careful studies revealed no evidence of acromegaly or hyperpituitarism. Yet a clear lesson is to be derived from these experiments, particularly with reference to patients who have a temporary exacerbation of diabetes during the course of infection. Thus, a young woman (Case 18978) thirty-eight years old required 124 units of insulin a day during severe pneumonia, yet two months later, during which period the insulin dose had gradually been reduced as the urine became sugar free, the blood-sugar values were normal and the diabetes had apparently disappeared. Of course this does not mean recovery, but the case will be watched. The effectiveness of insulin then during periods of infection or other temporarily increased strain on the islands of Langerhans may be, not merely to avoid acidosis and coma, but actually to protect the individual by resting the islands of Langerhans, and thus not only to prevent further damage to the islands, but even to allow for their return to normal.

### HYPOLYCEMIA

Hypoglycemia due to insulin continues to be a problem of major importance in the treatment of diabetes. In our experience 75 or 80 per cent of diabetic patients need insulin to enable them to utilize a satisfactory diet, of the 500,000 or 600,000 in the United States, it seems certain that at least 25 per cent, and possibly 50 per cent or more, actually take insulin. With all these an insulin reaction is an ever-present possibility. Pa-

tients must be informed of this fact at the beginning of treatment; they must be taught the causes, nature, symptoms and treatment of hypoglycemia. The facts must be presented without causing undue alarm and apprehension, fear of a reaction should never lead any patient to deny himself the benefit to be gained from insulin.

Fortunately, most individuals with diabetes are middle aged or elderly, and most of these have mild diabetes. Consequently the dosage of insulin is small and the chances of developing hypoglycemia correspondingly less. In addition patients vary in their sensitivity to insulin, and fortunately it is characteristic of the middle aged or elderly person with mild diabetes to be relatively insensitive to insulin and relatively tolerant of overdosage. Furthermore, most insulin reactions which occur in the course of the treatment of diabetes are mild and cause the patient relatively little inconvenience and no injury.

Despite these considerations it is true that some diabetic patients, particularly juveniles, are extremely sensitive to insulin, develop reactions with great ease, and may have symptoms of a most unpleasant and even alarming nature. Moreover, repeated, severe reactions in this relatively small group increase apprehension among patients at large, and serve to handicap not only the hypoglycemic offender himself but also other diabetic patients in obtaining and keeping jobs. No one can censure an employer who objects to the scene created in a busy office when a young diabetic employee suddenly develops a severe reaction with pugnaciousness, struggling, crying-out, convulsions and possibly unconsciousness. Only one rule can be established: severe reactions must not occur, or at least must not occur frequently. It is the duty and the responsibility of the patient, his family and his doctor to design treatment in such a way that severe reactions are reduced to the lowest possible minimum.

Reactions due to protamine zinc insulin may vary considerably from those brought on by regular or crystalline insulin. With the latter varieties, which are rapid acting, the onset of symptoms takes place in a few minutes and usually these consist of nervousness, sweating, tremor, faintness, rapid heart action and double vision. On the other hand, protamine zinc insulin acts so slowly that the onset of hypoglycemia may be insidious. Reactions after an overdose of protamine zinc insulin are commonest twelve to twenty-four hours after it has been given. If it has

been taken before breakfast, the commonest time for the reaction is between midnight and morning. Symptoms often include occipital headache, nausea and even vomiting, leading in some cases, therefore, to confusion in diagnosis with diabetic coma. My experience with protamine-zinc insulin has been the same as that reported by Lowrie and Foster,<sup>20</sup> who state that with their patients not only do reactions occur less frequently with protamine-zinc insulin than with regular insulin, but they are in general less severe.

Although there is no direct and absolute correlation between hypoglycemic symptoms and the level of the blood sugar, it is most uncommon to have symptoms unless the blood sugar falls to 0.07 mg per 100 cc or below. Most alleged cases of reactions at higher levels in reality represent false diagnoses, due either to the apprehension of the patient or to the fact that conditions other than hypoglycemia may cause any or all the characteristic symptoms. One exception to this rule may be granted when the blood sugar falls with extreme rapidity from a high to a considerably lower level, symptoms of a reaction may at times be felt without true hypoglycemia's being present. The level of blood sugar at which symptoms appear varies from patient to patient, and in the same individual from time to time. Thus, cases may be encountered in which no symptoms are present despite a blood sugar as low as 30 mg per 100 cc. It must be remembered that the blood-sugar methods in common use measure certain non-glucose-reducing substances which total from 15 to 25 mg per 100 cc, consequently, a value below 30 mg per 100 cc indicates that there is little or no true sugar in the blood.<sup>21</sup>

The important point in the diagnosis of hypoglycemia in an unconscious patient is to avoid confusion with diabetic coma. In the latter condition, large doses of insulin are life-saving, in the hypoglycemic patient they may well be fatal. The differential diagnosis is well known, and need not be repeated here. One cannot overemphasize the importance of seeking laboratory confirmation at once in doubtful cases, without knowledge of the blood-sugar level the physician may find himself treating the patient blindly and for the wrong condition.

It has now become well established that although body tissues in general may turn to protein and fat in time of need, nervous tissue has glucose as its sole food.<sup>22</sup> Consequently, when the blood sugar falls to extremely low levels and

the brain is deprived of sugar, cellular starvation results. Such a condition is incompatible with maintenance of the integrity of nerve cells. If profound hypoglycemia is long maintained, irreversible changes take place.<sup>23</sup> If this stage is reached, even though the blood sugar may subsequently be raised to normal, permanent damage to the nervous system may result. It is the experience of those giving shock treatments for schizophrenia that a small group of individuals remain in coma following cessation of a given treatment, even though the blood sugar has been raised to normal or supernormal levels.<sup>24</sup> In such patients both the immediate and the distant prognoses are grave.

The changes observed in the brain in fatal cases of hypoglycemia consist chiefly of tiny hemorrhages, multiple small thrombi, perivascular extravasations, interstitial edema and cortical necrobiosis affecting the ganglion cells.<sup>25, 26</sup>

In the treatment of diabetic patients the common causes of reactions are overdosage with insulin, failure to take the usual amount of food at the regular time or to assimilate it (vomiting, diarrhea), and unusual exertion. These suggest in themselves the important points in prevention. Insulin is a powerful preparation which must not be employed thoughtlessly. Although the dosage used must be determined largely by the method of trial and error, this should be done carefully and intelligently. Due thought should be given to the possible sensitiveness of the individual to insulin. With some patients, and particularly with children, with severe diabetes it may be found necessary to allow glycosuria and mild hyperglycemia at certain times during the day in order to avoid reactions at others. In the treatment of all diabetic patients, diet is fundamental, but in the patient receiving insulin it is more than ever important that the diet be uniform from day to day. With so many factors which are beyond one's control it is imperative that this influence be kept constant. Patients soon learn that if they take more than their accustomed amount of exercise a reaction may result. Consequently, whenever a change is made in the routine of living the possible effect on the insulin requirement should be considered in advance. It is a surprise each year to see with how much less insulin and how much more food diabetic children can be treated in summer camps where they are exercising daily out-of-doors than in the winter when activity is of necessity restricted. Before a period of any

unusual exercise patients should take a light lunch yielding from 10 to 20 gm of carbohydrate. Patients driving an automobile throughout the day should eat something every two hours. Patients receiving protamine zinc insulin should have a light lunch at bedtime. These lunches, designed for the prevention of reactions, should consist of food which requires digestion so that the effect on the blood sugar may be a sustained rather than a temporary one.<sup>37, 5</sup>

Mild attacks of hypoglycemia respond to relatively small amounts of food. Ten grams of carbohydrate as furnished by orange juice, ginger ale, sugar or candy usually suffices to overcome a reaction in five or ten minutes. More severe reactions, or reactions due to protamine zinc insulin, may require larger amounts of carbohydrate. In patients who are unconscious the injection of 20 cc. of 50 per cent glucose intravenously in a sterile buffered solution usually gives prompt relief. It is customary to terminate a shock treatment for schizophrenia by administering glucose solution by gavage. Glucose may be given in relatively large amounts in 5 per cent concentration subcutaneously or intravenously. Well-nourished individuals may respond to the subcutaneous injection of 0.5 cc. of adrenalin or pituitary extract.

The symptoms of hypoglycemia due to insulin are essentially the same as those due to hypoglycemia arising from other causes. Among the latter are undernutrition, exhausting physical activity, hypofunctioning of the pituitary, thyroid and adrenal glands, extensive disease of the liver, glycogen storage (von Gierke's) disease and hyperinsulinism. The last-named cause may reflect the presence of an islet-cell adenoma or carcinoma of the pancreas or, some have thought, generalized hypertrophy and overactivity of islet tissue without an actual tumor.<sup>38</sup> In all these conditions the treatment of the acute attacks is the supplying of food. To prevent recurrence specific treatment must be directed toward the underlying cause.

The paper of Campbell, Graham and Robinson<sup>30</sup> is of special interest because the features observed in their 5 cases are characteristic of those encountered in the treatment of patients with hyperinsulinism. In Case 1 an islet-cell adenoma was removed with apparent cure without incident, whereas in Case 2 it was not until a second operation that a tumor was found in the head of the pancreas its removal effected a cure. In Case 3 following removal of a tumor, the blood sugar became normal but the patient remained emotionally unstable and irritable and her memory and speech continued to be faulty, presumably because of

serious damage inflicted on the nervous system by the prolonged hypoglycemia prior to the operation. In Case 4 death took place on the third day after operation, at which splenectomy and partial resection of the pancreas were necessary in order to remove a tumor in the tail of the organ. In Case 5 no tumor was found and a resection of 34 gm of the pancreas was carried out. The patient had suffered no recurrence of hypoglycemia in the 10 months following the operation.

In reporting detailed studies in a patient with hyperinsulinism, Conn<sup>31</sup> mentions two practical points. The type of glucose-tolerance curve depends on the type of diet taken in the few days just preceding the test; a diabetic like response may be obtained if the carbohydrate intake has been low. Certain patients may be kept from extremely low levels and convulsions prevented if epinephrin is given twice daily subcutaneously.

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26271

## PRESENTATION OF CASE

*First Admission* A fifty-seven-year-old, Canadian-born, retired broker entered the hospital complaining of swelling of the ankles and abdominal enlargement.

He suddenly became aware of these symptoms, and also of dyspnea on exertion, two months before entry, on the day the firm by which he was employed went into bankruptcy. There was no pain. He slept poorly because of nervousness but was comfortable with one pillow and had no nocturnal dyspnea. A slight cigarette cough had been present and unchanged for many years. His appetite had progressively failed, but though food was distasteful there had been no nausea or vomiting. During the two months he gained approximately 10 pounds. Various pills and salts prescribed by his physician had provided no appreciable relief. On two occasions the penis became swollen for a short time.

The family history was non-contributory. The past history recorded a hemorrhoidectomy seven years and an appendectomy four years previously. On very close questioning the following data regarding alcoholic consumption were elicited and were considered reliable: from 1912 to 1927, ten drinks a week (a drink was defined as 2 oz. of whiskey or gin), from 1927 to 1929, fourteen a week, from 1929 to 1932, six a week, and from 1932 to 1938, four a week. The consumption was usually concentrated on the week end.

Physical examination showed a well-developed and nourished, sun-tanned man, lying flat in bed without discomfort. Examination of the eyes was negative, the tongue was coated, the throat injected. The heart was not displaced and showed no evidence of enlargement. The apex impulse could be clearly seen and felt, and shifted with change in position. There was no Broadbent's sign. The sounds seemed muffled and faint, there were no murmurs. The blood pressure was 130 systolic, 100 diastolic. The rhythm was regular, and the rate 80. The aortic second sound was equal to the pulmonary second sound. The radial pulses were equal and synchronous, and the peripheral arteries were negative. The diaphragms were high and fixed.

Dullness extended to just above the angle of the scapula on each side, the breath sounds were distant, and the spoken and whispered voice and the tactile fremitus reduced. Fine rales were heard over the dull areas. The abdomen was disproportionately large and showed shifting dullness, a fluid wave and early eversion of the umbilicus. The liver and spleen were not felt. There was bilateral pitting edema of the ankles and legs. Rectal examination showed a rosette of external hemorrhoids.

Six blood examinations showed hemoglobin concentrations ranging from 75 to 85 per cent (Tallqvist), red-cell counts from 4,600,000 to 5,000,000 and white-cell counts from 6000 to 13,000. The smear and differential counts were not remarkable. The urine showed specific gravities ranging from 1.004 to 1.030 and intermittent albuminuria (seven out of nineteen specimens). The sediment showed no red cells, variable numbers of white cells and, on occasion, hyaline casts. Three stools were guaiac negative. Two blood Hinton tests were negative. The nonprotein nitrogen was 20 mg. per 100 cc., the serum protein varied from 7.4 to 6.4 gm., in the latter specimen the albumin was 3.7 gm. and the globulin 2.7 gm. The serum chlorides were equivalent to 93 cc. of N/10 sodium chloride. The Takata-Ara and formol-gel tests were negative.

An electrocardiogram showed a rate of 90, normal rhythm, a PR interval of 0.14 second, low T<sub>1</sub> and inverted T<sub>3</sub>. The venous pressure in the left antecubital veins was equivalent to 60 mm. of water. The circulation time measured with saccharine (left arm to tongue) was 24.1 seconds. Abdominal paracenteses yielded abundant clear, straw-colored fluid, with a specific gravity of 1.018 and 1200 red blood cells and 250 white blood cells per cubic millimeter, a smear of the latter showed 9 per cent granulocytes, 38 per cent lymphocytes and 53 per cent large monocytes. Guinea-pig inoculation was negative for tuberculosis. Following the tap one examiner noted a poorly outlined mass in the epigastrium which descended with respiration, he could not feel the spleen.

X-ray examination showed a high diaphragm with good respiratory excursion. There was a small amount of fluid in each pleural cavity. The lower lung fields were poorly aerated. The heart was normal in size, the aorta slightly tortuous. Oblique views revealed nothing more. A gastrointestinal series, including an examination for esophageal varices, was negative. A barium enema showed scattered diverticula throughout the colon. A flat abdominal plate showed an area of calcification, 0.5 cm. in diameter, in the lower pole of the left kidney. A confirmatory intravenous pyelo-

gram showed prompt excretion of the dye on both sides and localized the stone in the left lower calyx.

In the hospital, despite fairly good response to Salyrgan and Mercupurin, the ascites tended to reaccumulate. Peritoneoscopy showed no evidence of malignancy. The liver was normal in color, the surface smooth. Six weeks after entry an exploratory laparotomy was performed with some reluctance on the part of the surgeon. The liver was considerably enlarged but smooth. A biopsy was taken. Careful exploration of the stomach and colon revealed nothing although adhesions from the previous appendectomy prevented palpation in the right lower quadrant. Pathological examination of the liver showed marked congestion and some atrophy of the liver cords in the centers of the lobule but no evidence of cirrhosis. One month later the patient was discharged with a clinical diagnosis of questionable cirrhosis.

**Subsequent Admissions.** During the next two years the patient re-entered the hospital twenty five times. The majority of these visits were overnight entries to the Emergency Ward for tapping but on four occasions he spent significant lengths of time on the wards. Despite Salyrgan every three days, tapping was necessary at least once a month and almost invariably temporarily relieved his symptoms.

Innumerable laboratory determinations were carried out. The hemoglobin concentrations and red-blood-cell counts fluctuated between 80 and 100 per cent and 4,000,000 and 5,000,000 respectively. The majority of white-cell counts fell between 6,000 and 10,000 and the blood smears were never remarkable. The ascitic fluid never changed significantly in character with specific gravities ranging from 1.011 to 1.018. Numerous examinations for tumor cells were negative. Van den Bergh tests hovered around 2 mg per 100 cc. Bromsulphaleins ranged from 35 per cent retention on the second entry to 20 per cent on the fourth, basal metabolic rates from -4 to -21 per cent. Fifty serum protein determinations varied from 4.79 to 7.4 gm per 100 cc., with a slightly downward trend but a marked weekly variation. The serum albumin ranged from 2.9 to 3.7 gm per 100 cc., and the globulin from 2.01 to 3.2 gm; the albumin globulin ratios varied from 0.98 to 1.72.

On several occasions, immediately after tapping, one or another member of the resident staff felt a non-tender midline epigastric mass which could be differentiated from the liver. Diagrams indicate that it was somewhat sausage-shaped and extended two thirds of the way from the ensiform to the umbilicus. The liver was frequently felt, the spleen never. Enlarged veins, which filled from below

after milking, gradually became apparent on both sides of the abdomen. Nine months after the original x-ray examination a repeat gastrointestinal series demonstrated definite esophageal varices. Repeated chest plates showed fluctuations in the amount of pleural fluid, no change in the size of the heart and no evidence of a mediastinal tumor. Another electrocardiogram showed normal rhythm, a rate of 105, a PR interval of 0.14 second, low T<sub>1</sub> slightly inverted T and T<sub>2</sub>, low voltage in all leads and slight left axis deviation.

Repeated transfusions with blood and with concentrated ascitic fluid failed to raise the serum protein level significantly and to delay the reappearance of ascites. He gradually grew more and more emaciated, but the hemoglobin concentration and red-cell count remained within normal limits.

**Final Admission** (twenty five months after the first symptom). The patient returned for abdominal paracentesis. Ten liters were removed with considerable relief, but he was still markedly dyspneic and examination revealed a large pleural effusion on the right side. Two thousand cubic centimeters of yellow slightly cloudy fluid was removed. He failed to rally, became gradually disoriented, finally comatose and died two weeks after admission.

#### DIFFERENTIAL DIAGNOSIS

**DR CHESTER S. KEEFER\*** The diagnosis in the present case must explain the recurrent ascites in a fifty seven year-old man who had an enlarged smooth liver and a heart of normal size. When these signs co-exist there are two main conditions to consider: *concretio cordis* and thrombosis of the hepatic veins. Before discussing these two conditions, it is well to review the important features of the case.

In brief, the patient first noticed swelling of the abdomen and legs two months before entry to the hospital. At the time of admission, examination showed ascites, a normal heart without signs of fixation and edema of the ankles and legs. The blood, the plasma proteins and the venous pressure in the arms were normal. The urine showed intermittent albuminuria, and the ascitic fluid had the characteristics of a transudate. A mass which descended with respiration was felt in the epigastrium. X-ray films showed a small amount of fluid in both pleural cavities. A gastrointestinal series was negative except for diverticulosis, and there were no signs of esophageal varices. There was a stone in the left kidney.

Exploratory laparotomy revealed a large liver,

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which in a biopsied specimen showed evidence of chronic passive congestion. No masses or other abnormalities were discovered.

The course of the illness was of interest in that he had rapidly recurring ascites over a period of twenty-five months, and in that the signs of obstruction of the inferior vena cava, as well as of portal obstruction, became more distinctive, as evidenced by the dilated veins on both sides of the abdomen and the appearance of esophageal varices. Later, a massive pleural effusion developed and the patient died.

At the beginning of the discussion, I stated that recurrent ascites with an enlarged, smooth liver and a heart of normal size always suggest concretion cordis or thrombosis of the hepatic veins, especially when one knows, as in this case, that a section of the liver showed chronic passive congestion. There are good reasons for excluding concretion cordis, namely, the shift of the heart with change of position and the normal venous pressure in the arms. Therefore, I am going to dismiss this diagnosis.

The second condition, namely, thrombosis of the hepatic veins, is rare, but one must explain the enlarged liver with chronic passive congestion, the recurrent ascites, the evidence of portal hypertension (esophageal varices) and, finally, the edema of the legs. Let us review some of the facts concerning thrombosis of the hepatic veins. In spite of its relative infrequency, there are a number of features of this disorder which are exceedingly interesting. In the first place the diagnosis may be extremely difficult or, in some cases, impossible during life since the clinical picture frequently simulates that of portal obstruction. Indeed, it may be associated with the latter. A diagnosis may be entertained if a patient has recurrent ascites and an enlarged, smooth liver with a convex surface, without signs of concretion cordis. This is especially true if a biopsy of the liver is obtained and shows chronic passive congestion.

Portal obstruction will also produce recurrent ascites, but in such cases the liver is usually small unless there is a tumor which has invaded the intrahepatic branches of the portal vein, in which case the liver is enlarged and irregular. Obstruction of the portal vein alone will not explain the clinical picture in the present case.

There are several features of this case which cannot be explained on a basis of hepatic-vein occlusion alone, in particular the edema of the legs and the pleural effusion.

The edema of the legs and the dilated veins on the abdominal wall naturally suggest that the obstruction was in the upper third of the inferior

vena cava as well as in the hepatic veins, that is, in that part of the cava where the hepatic veins enter.

The massive pleural effusion cannot be explained on the basis of obstruction of the inferior vena cava or hepatic veins. Naturally, this raises the question of the cause of pleural effusion in patients with liver disease. It may occur when there is an intercurrent tuberculosis of the pleura, a tumor of the liver with metastases to the pleuras or when there are low plasma proteins. In addition, it may be found when none of these conditions are present, especially when there is cirrhosis of the liver and hepatic insufficiency. This is a matter of great interest since Mann<sup>1</sup> found some years ago that partial excision of the liver was frequently followed by pleural effusion, an observation for which there was no adequate explanation. However, it is known that patients with hepatic insufficiency retain water, this has been ably demonstrated by Dr. Chester M. Jones.<sup>2</sup> It is possible, therefore, that the pleural effusion in this patient is associated, in some mysterious way, with the hepatic insufficiency.

If the clinical diagnosis of obstruction of the inferior vena cava and the hepatic veins is correct, then the question arises concerning its etiology. This condition has been observed in polycythemia vera, in tumors or infectious processes in the liver, in cirrhosis and in syphilis. There is no evidence for any of these conditions in this patient. Other cases have been described in which no definite cause for the thrombosis was found. In these it has been called endophlebitis obliterans hepatica. The process is frequently most conspicuous in the inferior cava about the mouths of the hepatic veins.

What about the possibility that a tumor had invaded the upper third of the inferior vena cava, thus causing this picture? This man was studied very carefully in an attempt to establish or exclude such a possibility. The tumors which invade the cava and occlude the hepatic veins as well are hypernephroma, tumors of the liver or of the testis and, rarely, tumors of the pancreas. At the time of operation no tumor was found. However, there is the recorded observation that a non-tender, midline, epigastric mass was felt which could be separated from the liver. Evidently this appeared after the exploratory operation and could be felt only after tapping. This may have been a tumor or a rolled-up, thickened omentum. In any event, I cannot explain it. It would seem unlikely, however, that a tumor of this size could have been overlooked at the time of operation, so that we do have to assume that it appeared following it. It

seems to me that the most likely diagnosis is an obstruction of the inferior vena cava and hepatic veins by a thrombus. I am, however, unable to make an etiologic diagnosis. My final diagnosis, then, reads obstruction of the inferior vena cava and hepatic veins, with chronic passive congestion of the liver, esophageal varices, pleural effusion.

DR. TRACY B. MALLORY: Are there any questions or alternative diagnoses?

DR. HOWARD C. COGGESHALL: I was wondering about the spleen. Did the absence of splenomegaly influence you in making your diagnosis?

DR. KEEFER: The absence of splenomegaly is difficult to explain inasmuch as he had signs of portal obstruction, but in an individual fifty-seven years of age with portal obstruction the spleen is frequently not enlarged. Certainly you do not find it enlarged in more than about 50 per cent of the cases. I think there was enough evidence without splenomegaly to make the diagnosis of portal hypertension.

#### CLINICAL DIAGNOSIS

Cirrhosis of liver

#### DR. KEEFER'S DIAGNOSES

Obstruction of the inferior vena cava and hepatic veins with chronic passive congestion of the liver

Esophageal varices

Pleural effusion

#### ANATOMICAL DIAGNOSES

Neurogenic fibrosarcoma of the inferior vena cava, occluding it from the mouths of the renal veins to the right auricle

Cardiac cirrhosis of liver

Esophageal varices

Thrombosis of iliac veins and lower 3 cm of vena cava

Pleural effusion, right.

Ascites

Operative scars: appendectomy, omentopexy, multiple paracentesis

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: This case is a unique one, and I think Dr. Keefer has come as close as is reasonably possible. I can remember having a long discussion as to the clinical diagnosis at the time of the first biopsy of the liver, and my reasoning ran very close to that of Dr. Keefer. I argued that one had to place the obstruction in the cava close to or perhaps above the mouths of the hepatic veins and that if as seemed to be the case, constrictive pericarditis could be ruled out there must be thrombosis of the inferior vena cava of one sort or another.

One other possibility also occurred to me, namely, that there might be a tumor of the left auricle so located that it would obstruct the mouth of the inferior without obstructing the mouth of the superior cava.

The autopsy presented a most confusing picture. The surgeon, who as has been said explored the



FIGURE 1

*The vena cava has been opened from behind showing the tumor extending upward to the point of section just below the auricle. The extracaval portion of the tumor lies to the left partially covered by the aorta. The iliac vessels and the cava just above their union contain thrombi.*

case reluctantly, did an omentopexy despite the fact that there was no cirrhosis, and as a result all the organs were rolled up in omentum and dissection was very difficult. It soon became apparent that the vena cava was distended to an enormous degree. It measured about 5 cm in diameter and felt quite solid. On opening it we found a long sausage-shaped tumor, 20 cm in length which was lying for the most part free in the lumen but was attached to the lateral wall of the cava at about the level of the celiac axis (Fig 1). At that point the tumor passed through the wall of the cava and out into the retroperitoneal tissues where another similar mass of almost but not quite equal size was present. So we had a dumbbell-shaped mass about half in and half outside of the cava. The tumor extended high enough to overlie the

mouths of the hepatic veins, which were stretched so taut that we had considerable difficulty in finding them, so I felt quite certain that there was obstruction at that point. The tumor actually extended 10 or 20 cm into the right auricle. The liver, by the time of autopsy, had become somewhat smaller than it was when first observed. It was very slightly granular and was quite definitely tough. Microscopic examination of the liver post mortem showed well-marked cirrhosis of the so-called "cardiac type," which was not present in the biopsied specimen. The intervening two years of constant passive congestion explain the development of this type of cirrhosis during the period of observation. If I understood Dr. Keefer correctly he assumed that the obstruction to the hepatic veins occurred first and the caval obstruction later. The anatomical findings clearly indicate that the obstruction must have occurred in the reverse order. I believe that this is also borne out by the history, since the first really unequivocal evidence of hypertension in the portal circulation was the appearance of esophageal varices late in the disease, varices which were looked for and not found two years before. The tumor, itself, was a very slowly growing, spindle-cell sarcoma, I thought in all probability a neurogenic fibrosarcoma. Whether it was primary in the wall of the cava or started in one of the sympathetic ganglia in contact with the cava I cannot say.

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### CASE 26272

#### PRESENTATION OF CASE

A twenty-year-old girl was admitted to the hospital complaining of dyspnea.

Two and a half years before admission the patient developed amenorrhea. She consulted her physician, who discovered the presence of diabetes and placed her on a diabetic diet. Her catamenia became normal again. She was sugar-free and apparently well under this regime for six months, when she became acutely ill, with severe headaches, dyspnea and anorexia. She became stuporous, and then comatose, and was placed in an outside hospital for a two-week period, where she was given a restricted diabetic diet with 20 units of insulin three times a day. On this regime she remained well until about two weeks before admission, when she developed a severe sore throat. Benedict's test for urine sugar became red, and the insulin dosage was raised to 25 units three

times a day for a period of one week. Along with the sore throat there also occurred an elevated temperature, malaise and weakness. In addition her physician discovered high blood pressure. The sore throat persisted for one week, during which time an abscess in the right ear canal developed, which ruptured spontaneously. At about the same time she developed what she described as a papular rash over the face which persisted for some five days and then gradually disappeared. The next day, however, the ankles and both legs became edematous and she experienced chilly sensations. She had no other complaints until six days before admission when the peripheral edema increased and became evident over the body, face and upper extremities. Since that time the edema persisted. Five days before entry she developed a nonproductive cough, which prevented her from sleeping in the supine position. Symptomatic therapy by her physician failed to relieve the symptoms. She became thirsty and required large amounts of water. In spite of this, urinary excretion became less so that she urinated only four times in twenty-four hours and in small amounts on each occasion. The urine was sugar free, but for two days before hospital admission she noted that a white flocculation appeared while heating it. Three months before admission the patient weighed 123 pounds, at which level she had remained until one week before admission, when over the seven-day period she gained some 26 pounds. During her illness she did not complain of pain, night sweats or epistaxis.

As a child she had had chicken pox, pertussis, measles and tonsillitis, and about one cold with sore throat a year. There was a history of diabetes in a maternal aunt, a grandmother and a great-aunt. Her father, mother and two sisters were living and well, without symptoms of diabetes.

Physical examination revealed a pallid, puffy girl sitting bolt upright in bed, having marked dyspnea and orthopnea with a constant hacking, nonproductive cough. There was generalized pitting edema of the extremities, the trunk and the face. Examination of the retina revealed tortuosity of the arteries, out of proportion to her age, with marked arteriovenous nicking but no exudate or hemorrhage. The neck veins were moderately distended. The lungs were dull to percussion in both axillae and at both bases, with decreased tactile fremitus, breath sounds, whispered voice and spoken voice. There were multiple consonant rales heard about these levels on both sides, no friction sounds were audible. The heart was enlarged, the area of dullness extending 2 cm beyond the midclavicular line in the fifth left interspace,

with a heaving, rapid apical impulse at a rate of 128. The sounds had a gallop rhythm. No definite murmurs were distinguished. The pulmonary second sound was slightly louder than the aortic second. The blood pressure was 168 systolic, 130 diastolic. The abdomen was edematous with moderate ascites. The spleen was not felt, but the liver edge was palpable two fingerbreadths below the costal margin in the right midclavicular line and was tender. The tourniquet test was positive.

The temperature was 100°F, the pulse 136 and the respirations 35.

Examination of the blood showed a red-cell count of 3,900,000 with 70 per cent hemoglobin and a white-cell count of 9600 with 81 per cent polymorphonuclears, 18 per cent lymphocytes, and 1 per cent monocytes, the smear was normal. The urine was dark amber, with an acid reaction, the specific gravity was 1.029, with a +++++ test for albumin, a green sugar test and no diacetic acid or acetone, the sediment showed 10 to 20 red cells, 5 to 10 white cells and many finely and coarsely granular casts per high power field. The carbon dioxide combining power was equivalent to 22.5 cc of N/10 sodium bicarbonate per 100 cc. The total cholesterol was 185 mg per 100 cc., the whole-blood nonprotein nitrogen 22 mg., and the blood sugar 130 mg.

The patient was given morphine for sedation and was rapidly digitalized both intravenously and by mouth, and fluids were permitted to aid in overcoming anuria. She was given insulin and was placed on a diabetic dietary regime. There was an apparent improvement in the general condition during the first twenty-four hours of her hospital stay but she failed suddenly and expired on the second day. Immediately before death she was found to have had the following blood findings: carbon dioxide combining power 22 cc. of N/10 sodium bicarbonate per 100 cc. chlorides, 35.9 cc. of N/10 sodium chloride per liter nonprotein nitrogen, 28 mg per 100 cc., protein 6.3 gm, total base 156.7 milliequiv.

#### DIFFERENTIAL DIAGNOSIS

DR. BERNARD M. JACOBSON. We are faced in this case with a combination of diabetes and hypertension a situation that is not very commonly seen in a young person. It certainly is rare moreover, for a person of this age to die, the way this girl died, of severe cardiovascular renal disease without more typical findings of glomerulonephritis. It is interesting that two and a half years before entry she developed amenorrhea and diabetes was found. One wonders momentarily whether this girl developed a Cushing's syndrome,

but as subsequent events turned out, it is evident she did not. Her periods came back, and the diabetes was easily controlled. There is nothing on subsequent physical examination to suggest a Cushing's syndrome. Apparently over a period of two years the diabetes could not be called very severe. We do not know about the blood sugar levels during this period. It was only two weeks before admission that the first mention was made of the presence of hypertension.

The present illness followed a respiratory infection and sore throat two weeks before admission, and six days before came the onset of edema, at first slight and then rapidly generalized, involving the trunk and extending up to the face. Orthopnea became marked twenty-four hours before entry. It is mentioned that although the urine was sugar free a white flocculation appeared on heating with Benedict's solution. That undoubtedly must mean the precipitation of urates due to concentrated urine, and certainly such a highly concentrated urine speaks for good kidney function, so far as excretion of solids goes. There was a remarkable gain of weight, — 26 pounds, — presumably due to edema, during the week before entry.

Physical examination revealed findings indicative of hypertension, hypertensive heart disease and subsequent myocardial insufficiency. The clinical signs of congestive heart failure were present, and the fact that the patient ran a very rapid pulse rate with gallop rhythm is certainly indicative of a very severe degree of myocardial insufficiency. When a person of this age goes into decompensation with abnormal rhythm it is indeed a grave omen. One additional finding besides those of congestive heart failure is the presence of edema of the upper part of the body. The patient was pallid and puffy certainly findings that should attract our attention. They are not typical of congestive heart failure of the ordinary types, and they are important findings for further diagnosis. The note about the tourniquet test has no pathognomonic significance. We are not told about the presence of the free fluid in the chest by x-ray. I doubt from the physical signs if there could have been much although there apparently was a slight pleural effusion. The blood showed mild secondary anemia and nothing remarkable in the white blood cells. The urine gave a +++++ test for albumin and other positive findings, which by themselves are not diagnostic. Certainly we see such urinary sediments and that much albumin in cases of severe cardiac decompensation without any significant degree of renal disease. It is interesting that the blood chemical findings were

normal. The serum protein was almost normal, and probably was slightly lowered merely by the albuminuria. We are not told whether the patient was given diuretics during the first twenty-four hours in the hospital. She probably was, with this much edema. Certainly the activity of the diabetes at the time of entrance to the hospital was not very great.

The rather sudden death suggests left-sided heart failure, possibly after the development of an abnormal rhythm. I do not believe that we learn anything more from the final blood determinations. The patient did not have diabetic acidosis or decompensated renal function. I am certain that the patient had diabetes mellitus, and hypertension, probably of long duration because of the size of the heart and because of the presence of definite arterial changes in the retinas, both tortuosity and marked arteriovenous nicking. There is no question she had myocardial insufficiency, which probably was the immediate cause of death.

We come to the question of what was going on in the kidneys. I think we cannot dismiss the type of edema that was present, its distribution in the upper part of the body, including the face, was very marked and noted by the patient and on physical examination on entry to the hospital. This type of edema suggests the question of whether this patient had some type of tubular change in the kidneys or whether the patient was in a nephrotic stage of glomerulonephritis or possibly was suffering from lipoid nephrosis. As I have said, the amounts of albumin in the urine and the sediment are still consistent with severe congestive heart failure. We have no history of acute glomerulonephritis in the past to suggest that this might be a subacute glomerulonephritis with edema. Certainly the amount of sediment in the urine is not enough to suggest acute nephritis, unless other urine examinations were done. Ten to 20 red cells and 5 to 10 white cells in the sediment are not consistent with an acute glomerulonephritis that came on two weeks after a respiratory infection and terminated in death.

DR. TRACY B. MALLORY. There are three urines recorded, with the specific gravity ranging from 1.028 to 1.033 and a ++++ test for albumin in all, there were 5 to 7 red cells on one occasion, and 10 to 20 on another, and they are reported as "crowded" on the third, white cells were always present.

DR. JACOBSON. Against acute glomerulonephritis is the fact that this patient must have had a hypertension of at least several years' duration prior to the onset of the terminal illness. Despite the absence of the history is this possibly a subacute glomerulonephritis? I have no way of telling ex-

cept for two factors. The patient had a normal blood cholesterol, and not a very markedly depressed serum protein. I think it is fair to say that this is not a typical nephrotic syndrome, despite the distribution of the edema. Once in a while we run into a nephrotic syndrome, some what imperfect, in the presence of other conditions in the kidney, such as amyloid disease. Certainly from the past history we have no evidence to suggest that this is amyloid disease.

I have mentioned the diagnoses that I think are certain. There is one other possibility which I see no way of proving, except to await Dr. Mallory's report. In the past few years there have been described in the literature several cases of a syndrome termed "diabetes mellitus, hypertension and intercapillary glomerulosclerosis." This was a syndrome first described by Kimmelstiel and Wilson<sup>1</sup> in 1936, one case has been reported by Derow, Altschule and Schlesinger<sup>2</sup> at the Beth Israel Hospital, Boston, and others by Newburger and Peters<sup>3</sup> at New Haven. All the cases reported had diabetes of several years' duration, all had hypertension, all had arterial changes in the retinas, and all had something pointing to disease in the kidneys. Some had the complete nephrotic syndrome, including low serum protein and high blood cholesterol values, but others lacked these characteristic blood chemical findings. At autopsy all these cases had the signs of long-standing hypertension and a rather high degree of sclerosis of the small arteries especially in the kidneys, with a very high degree of diffuse fibrosis of the central glomerular tufts with extension toward the periphery, many cases had, in addition, tubular changes of one sort or another. These were changes that these authors believed could be distinguished from those of ordinary active or healed subacute glomerulonephritis. I have never seen such a case, but it is my guess in this patient in order to explain the entire picture. I list my diagnoses as diabetes mellitus, hypertension, hypertensive heart disease with cardiac failure, and intercapillary glomerulosclerosis.

DR. EDWARD F. BLAND. Dr. Jacobson mentioned that he believed the hypertension must have been present for several years. I wonder why? Because of the eyegrounds?

DR. JACOBSON. Yes, and because the heart was considerably enlarged.

DR. BLAND. Of course the heart in young people can enlarge very quickly.

DR. MALLORY. A few years ago Dr. Earle M. Chapman studied patients with acute glomerulonephritis, and quite marked enlargement of the heart was demonstrable by x-ray in several which

disappeared in a few weeks as the renal disease subsided

DR. BLAND They see this picture at the Children's Hospital in patients with acute nephritis, but usually there is more evidence of acute nephritis

DR. JACOBSON We know that the hypertension existed for at least some time before she entered and before the edema appeared

DR. BLAND The patient did have a sore throat followed quickly by heart failure, so that we can not forget diphtheria. It is very unlikely here, but we have to think of it.

DR. JAMES H. THIVENSEN I have seen vascular disease in young diabetic patients, but it usually takes at least ten years of known diabetes to produce severe vascular disease at the age of twenty. I think it is probably fair to assume that the diabetes did not exist in this case more than two and a half years, because at this age diabetes makes itself manifest by symptoms soon after it begins. I have never seen extensive vascular disease develop in that length of time in a patient treated adequately, such as this patient seems to have been. I should be surprised if the postmortem showed generalized arteriosclerosis. My impressions from seeing her were that the diabetes probably had very little to do with the situation and that she developed an acute nephritis in the same way any non-diabetic patient might. Possibly because she was diabetic and since her resistance to infection was poor, she may have had a severer acute nephritis. Certainly all the edema was not cardiac, because she had it in the face and eyes and upper part of the body. The mode of death certainly was cardiac. She died with a dilated heart. Whether one can do that from acute nephritis I do not know, but I have the impression that one can die from cardiac failure in nephritis with edema, and this girl was terrifically edematous.

DR. PAUL D. WHITE I have very little to add to Dr. Jacobson's excellent discussion. We were greatly disappointed in the patient's failure to recover from the congestive failure, for she was improving when she died suddenly. We could not explain the death, but thought of a possible abnormal heart rhythm.

It was evident from the history that the sore throat episode was the vital factor precipitating the illness that ended in death three weeks later. We were inclined to think that the kidneys must have played an important role because of the clinical findings, despite the normality of the renal function tests.

One does see edema of the arms and face, es-

pecially unilateral, in congestive heart failure alone, but we thought that the kidneys entered the picture because of the high degree of bilateral edema of the face and arms.

#### CLINICAL DIAGNOSES

Diabetes mellitus.  
Acute nephritis  
Cardiac dilatation with decompensation  
Generalized anasarca  
Pulmonary edema  
Bilateral hydrothorax  
Ascites?

#### DR. JACOBSON'S DIAGNOSES

Diabetes mellitus  
Hypertension  
Hypertensive heart disease.  
Acute cardiac failure.  
Intercapillary glomerulosclerosis

#### ANATOMICAL DIAGNOSES

(Diabetes mellitus)  
Acute intracapillary glomerulonephritis  
Hypertrophy (slight) of the heart.  
Acute cardiac failure.  
Acute pulmonary edema  
Anasarca

#### PATHOLOGICAL DISCUSSION

DR. MALLORY This girl had two potentially lethal diseases but I do not believe she died directly from either of them. The diabetes was perfectly controlled during the last few days of the illness, and she certainly did not die of renal insufficiency, at least not of uremia. But she did have acute nephritis. The kidneys were large and swollen, and nearly all the glomeruli showed definite intracapillary proliferative changes, probably not sufficiently severe, however, to produce uremia. Nevertheless, I think indirectly nephritis was the cause of death. Longcope<sup>4</sup> has very recently emphasized the frequent appearance of cardiac failure in patients with acute nephritis. Severe, almost paroxysmal, hypertensive symptoms may appear quite early in acute nephritis. He considers them at least in part responsible for the acute cardiac failure which he has frequently observed. Coming back to this patient there was a pleural effusion of 700 cc. on the right and one of 200 cc. on the left. The lungs were extremely wet and heavy and markedly edematous and on anatomical grounds the best explanation of death is sudden left ventricular failure.

I am glad Dr. Jacobson brought up the question of intercapillary glomerulosclerosis, which should certainly be seriously considered in any

patient with the combination of hypertension, diabetes and a nephrotic syndrome. So far as I know, however, this condition has never been reported in a patient as young as this. The typical patients are usually around fifty.

DR. JACOBSON: I think the youngest one reported was forty.

DR. MALLORY: The age was the strongest point against that diagnosis, although it was a perfectly reasonable one to suggest.

DR. TOWNSEND: Did she show any generalized vascular disease?

DR. MALLORY: Virtually none. The heart was only slightly hypertrophied, weighing 350 gm. So I do not believe she had chronic hypertension.

DR. JACOBSON: I was thrown off by the eye-ground findings.

DR. TOWNSEND: Presumably they developed during the acute illness. I wonder if the nicking was not due, to a certain extent, to venous engorgement. She certainly had a great deal of generalized venous engorgement. The early history illustrates a mistake that is very often made with young diabetic patients in trying to manage them on a diet alone. They nearly always do the same thing in about six months; they will be in trouble of one type or another if one tries to manage them without insulin.

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# The New England Journal of Medicine

Formerly the  
Boston Medical and Surgical Journal  
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND  
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE  
ON PUBLICATIONS

Official Organ of  
THE MASSACHUSETTS MEDICAL SOCIETY  
THE NEW HAMPSHIRE MEDICAL SOCIETY  
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**SUBSCRIPTION TERMS:** \$6.00 per year in advance, postage paid, for the United States; Canada, \$ 04 per year; \$8.52 per year for all foreign countries belonging to the Postal Union.

**MATERIAL** for early publication should be received not later than noon on Saturday.

The Journal does not hold itself responsible for statements made by any contributor.

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## RESULTS IN THE CAMPAIGN AGAINST SYPHILIS

The medical profession—and laymen as well—will be interested in the results of the campaign waged against syphilis under the sponsorship of Surgeon General Parran and the United States Public Health Service. The report\* for the year 1939 reviews these results and indicates great progress.

The fact that 103,000 patients were discharged from clinics in 1939 as cured or with syphilis arrested, as compared with 78,000 in 1938, is most gratifying. Sixty per cent more persons were brought under treatment for the first time in 1939, and 65 per cent more treatments were given in clinics. Treatment and laboratory facilities increased between 30 and 85 per cent in the various

states, and tests for syphilis showed a marked increase. More states set up separate divisions for venereal disease control, and more full-time health officers were employed. Nineteen states now require examination and serological tests for syphilis for marriage licenses, and fifteen require prenatal tests. Educational projects for physicians and laymen have been greatly expanded. Nine leading universities have established teaching centers for the training of physicians and nurses in the care of patients with venereal diseases, and research activities in various phases of the subject have been initiated or continued. Follow-up work has improved, and patients are made to feel the necessity for regular and adequate treatment. When figures are available, congenital infections will undoubtedly be found to be greatly decreased.

A combined attack against a major and incapacitating disease is being developed, and there is no reason for doubting that it will be successful, as have attacks in the past against smallpox, malaria, typhoid fever and yellow fever. With increased funds appropriated for the present year, and the experience and impetus given by the campaign thus far, it is reasonable to expect that a major victory will be achieved in this field of medicine.

## WASHINGTONIAN HOSPITAL

On November 5, 1841, the present Washingtonian Hospital was organized as the Home for the Fallen, and on March 26, 1859, was incorporated as the Washingtonian Home and endowed as a place of treatment for alcoholic patients. It fulfilled a necessary function without any change of policy until 1939, when, due to the energy of Dr. Hilbert F. Day, an entirely new policy was projected which gradually became operative. The change was symbolized by the adoption of the name, Washingtonian Hospital. More concretely, a staff of visiting physicians in neurology and psychiatry made up of Drs. Leo Alexander, Wilfred Bloomberg, Robert E. Fleming and Merrill Moore was organized, daily visits are being made, and research and modern treatment have been instituted. The resident staff was altered, and now consists of Dr. Charles Parsons, superintendent, and Dr. Jos

\*Progress in venereal disease control during the fiscal year 1939. *Yew Dis. Inform.* 20:376-378, 1939.



eph Thiman, resident physician. A woman nurse has been placed in charge of the nursing. The consulting staff is made up as follows: dermatology, Dr. Perry C. Baird, Jr., internal medicine, Dr. Maurice B. Strauss, neurosurgery, Dr. William Jason Mixer, pathology, Dr. Harold A. McMahon, psychiatry, Dr. Abraham Myerson, surgery, Dr. Hilbert F. Day. Thus, medical activity of a modern type is being brought to bear on the problem of alcoholism.

The hospital asks for the support of the medical men of Metropolitan Boston in order that it may continue to grow and become an important factor in the understanding and treatment of alcoholism, which is now recognized as one of the major problems of modern society. Follow-up care will be given, and an outpatient department, which has the support of the Commissioner of Mental Health, Dr. Clifton T. Perkins, is in the process of development.

The aim of the hospital is to be of service to the alcoholic patient, to help the doctor in his care of these perplexing and difficult cases, and to advance the knowledge of the causes and treatment of alcoholism.

## MEDICAL EPONYM

### CHARCOT JOINT

Jean Martin Charcot (1825-1893) described "quelques arthropathies qui paraissent dépendre d'une lésion du cerveau ou de la moelle épinière [certain arthropathies apparently dependent on a lesion of the brain or spinal marrow]" in the *Archives de physiologie normale et pathologique* (1:161-178, 379-400, 1868). A portion of the translation follows:

We may summarize briefly the outstanding characteristic of the joint condition which we have observed in several ataxic patients. First, we again emphasize the absence of any external cause, traumatic or otherwise, any diathesis or constitutional influence to which it may be attributed. Syphilis, gonorrhea, the rheumatic or gouty diathesis, the prolonged effect of cold and moisture either could not be blamed, or else were completely absent in the previous histories of our patients. So far as the localization is concerned, the arthropathy involved impartially either knee, sometimes the right, sometimes the left, and in one case the left elbow. The absence of fever, redness and pain seemed an almost constant characteristic.

Swelling was always pronounced in the region of the joint itself, the principal cause being the accumulation of a certain amount of fluid in the synovial cavity, but at the same time the adjacent parts were constantly involved, sometimes over an extensive area. Digital pressure left no pitting. In all cases the condition improved spontaneously and progressively, but nearly always there were lesions which generally persisted, and which in one case were so marked as to cause a true dislocation of the joint.

R W B

## OBITUARY

### GEORGE GRAY SEARS

1859-1940

George Gray Sears was born in Boston on October 22, 1859, and died there on May 28, 1940. His parents were George O. and Sarah G. (Richards) Sears. On February 2, 1904, he married Ruth Williams, of Boston. He had two daughters, one daughter, the wife of Dr. Richard Chute, of Boston, survives him. Except for his college days at Amherst, his eighty years of life were spent in Boston.

Additional facts in the chronology of his life are as follows: A.B. in 1880 and Sc.D. (hon.) in 1925, Amherst College; M.D. cum laude in 1885 and LL.D. in 1926, Harvard University; medical house pupil at the Massachusetts General Hospital, 1884-1885; district physician, Boston Dispensary, 1887-1889; outpatient physician, Carney Hospital, 1887-1889; visiting physician, Channing Home, 1891; physician to outpatients, 1893-1895; assistant visiting physician, 1895-1903; visiting physician, 1903-1919; trustee, 1918-1939, Boston City Hospital; trustee, Forsyth Dental Infirmary, 1924-; assistant, 1893-1897; instructor, 1897-1901; assistant professor, 1901-1911; associate professor, 1911, of clinical medicine; clinical professor of medicine, 1912-1918; professor of clinical medicine, 1918-1919; emeritus professor, 1919-; Harvard Medical School.

The facts of the life of George Gray Sears just enumerated form a silhouette but lack the details of line and color necessary to a portrait of the man as he lived and worked in the Boston community. What sort of a man was he? Not dynamic, not dramatic, never erratic, a quiet man of restrained mien, forceful, alertly watchful of his surroundings, never loquacious, able with few words, sometimes with a single word, to give the idea he wished conveyed, somewhat cynical at times, seemingly for its effect rather than expressive of his real self, tall, at no time either lean or

fat, with keen, kindly eyes and an evanescent smile playing about his mouth, a man that would be noticed in any gathering, a lovable, delightful companion to those who knew him well, filled with the wisdom that comes from observation and experience of men and matters, such was George Gray Sears. In his quiet, unobtrusive way he went through life busied with the practice of medicine, with teaching, with hospital visits, with trustee meetings, with interviews, all part of the work of a man whose concern broadly was with men, with institutions, with public affairs.

For forty-six years he labored at the Boston City Hospital in a period of phenomenal growth in number of patients, in size and quality of plant, in extension and improvement of the medical care of those who there sought cure of their disease and succor from their suffering, and in the development of scientific study of disease. For twenty-six years he was a member of the clinical staff, for twenty-one years a trustee. When he retired as trustee, the senior staff presented him with an engraved testimonial signed by every member of the senior staff. This, among other things, it had to say of him:

A gentle and lovable physician—a distinguished teacher, a wise administrator. A gentleman learned and scholarly—a large part of whose busy life was diligently devoted to the hospital he loved. He served faithfully through all the grades of the staff from the lowest to the highest. His thorough knowledge of the professional problems of the hospital brought a fine balance to the Board of Trustees and was of invaluable aid in the solution of its difficulties.

At the Harvard Medical School he served actively for twenty-six years, progressively advancing from assistant to professor of clinical medicine. In sections he taught auscultation and percussion, on ward rounds he conducted clinical exercises, in the amphitheatre he held clinics or lectured. In showing to the students the way of making the correct diagnosis and directing the treatment of patients, he excelled.

In both institutions, as with patients, colleagues and friends, his part was to advise when asked for advice, to guide a movement already under way rather than to provoke its start. And yet he was not unprogressive, not lacking in initiative, not failing to look far into the future of medical developments. It was his way of getting things accomplished to give advice to the right person at the right time, to retard or to accelerate some movement by coming into its discussion at just the time his quiet, sage advice was needed, when before this, he had listened and learned put in an

occasional query, but said very little. Few knew the many important things that were accomplished by him in this way, for he talked but little of what he had done, that they were many is made probable by a casual remark to patient or friend that occasionally, almost by accident, slipped out to indicate the part he had played in some development in Boston.

George Gray Sears was an ideal practitioner of medicine. He was an accurate observer, skillful in physical examination, inspiring in his patients that confidence which led them to divulge to him the intimate details of life and its reactions, facts so necessary for an understanding of disease as it affected that particular individual. Understanding his patients as he did and having their complete confidence, he became for them a wise adviser, not alone in matters of health but in all that concerned their daily lives. To his colleagues in medicine he rapidly became a valued consultant for their patients, and they sought his help and advice in the solution of many personal problems. To the younger physicians he was an example of the ideal practitioner.

A life filled with usefulness to patients, colleagues, friends and the community has ended. The memory of George Gray Sears long will remain as a benison to many.

HENRY A. CHRISTIAN

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

RAYMOND S. TITUS, M.D., Secretary  
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#### INFLUENZAL PNEUMONIA DURING PREGNANCY

Mrs. K., a twenty-one year-old primipara about thirty-six weeks pregnant, was seen in consultation on September 13, 1918, because of fever and prostration.

The family history was essentially negative. The patient gave a negative history. Catamenia began at twelve, were regular with a twenty-eight day cycle, and lasted four days without pain. The last period had started on January 2, making the expected date of confinement October 9.

The pregnancy had been normal up to forty-eight hours before the patient was seen. At that

\* A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

time she developed a cough and the temperature was 101°F, and the pulse 120

Examination disclosed a well-developed and well-nourished young woman sitting up in bed. The respirations were embarrassed, the color was poor, the patient being slightly cyanotic. Rales were heard in both lungs. The heart was not enlarged, there were no murmurs. The blood pressure was 110 systolic. The uterus was enlarged to the size of an eight months' pregnancy, with the vertex presenting and the fetal heart audible. The uterus was not contracting. Although the patient did not seem seriously ill, a very guarded prognosis was given after a diagnosis of influenzal pneumonia had been made. It was advised that the patient be left alone, and be treated symptomatically and conservatively.

Three days later the membranes ruptured spontaneously and labor started immediately. The progress of labor was normal, and the patient was delivered normally, gas and oxygen being used as an analgesic and anesthetic. The baby was premature and rather slow to breathe, but lived. The patient's temperature came down to normal two days after delivery and remained so.

*Comment* In the epidemic of 1918, influenza during pregnancy was a very serious complication. Some patients died undelivered, others were delivered and died. The question of inducing labor was frequently brought up only to be rejected, because it was believed that any operative procedure was contraindicated. The prognosis was grave and depended much more on the virulence of the infection than on any other single factor.

#### ARE VACATIONS NECESSARY?\*

A well known physician made the statement on one occasion that a man could do an excellent year's work in eleven months but not in twelve. This is simply a variation on the old theme that all work and no play makes Jack a total loss sooner or later, and what applies to Jack is equally true of Jill. The tired, nervous housewife and the hard driving business executive may both be headed for serious trouble if they do not occasionally call for "time out." Business and industry have to a great extent recognized the fact that not only is health served but efficiency is promoted by the granting of a vacation.

Before going any farther I should like to explain what a vacation really means. Anything which will give us mental and physical relaxation from the work which occupies us the year round can properly be called a vacation. It means forgetting our work, forgetting our cares and forgetting our scramble for greater wealth. Above all it should give us the opportunity to play and have some fun, both of which many adults have lost the ability to do, because of constant work, constant worry and constant ten-

sion over a period of many years. It should also mean a complete change of environment, because the cares and worries of everyday life drop away much more easily in new surroundings. And finally it should also mean a change in our usual type of activity. Much fun has been made of the mailman who spent his vacation hiking, the sailor who went boating, and the truck driver who took a cross-country automobile trip. On the other hand, the change in activity which is so advisable must not be carried to any unusual extremes. The young woman who has teetered through fifty weeks on four-inch French heels and suddenly puts on moccasins for long walks through woods and ravines, or the salesman who has spent most of his waking hours behind the wheel of an automobile and suddenly decides to climb seven mountains during his two-weeks-off may be in for a good deal of trouble because they have not taken into consideration that the human body may not be able to adapt itself to such violent changes of environment.

People who need vacations most frequently raise the objection either that they cannot afford one or that their work does not permit them to leave it for any length of time. Concerning the first objection, the matter of expense, aside from those unfortunate enough to barely eke out a living or slightly more, this question is usually not so forbidding as it appears. In the first place, with a little ingenuity, vacations involving very little expense can be arranged. And secondly, I am quite certain that the improvement in one's health which a proper vacation produces is not measurable in terms of dollars and cents. The amount of money thus saved on doctors' bills may help finance part of the vacation. To those who believe that their work cannot get along without them, I must repeat what has so often been said, that none of us are indispensable, particularly fifty-two weeks out of every year, and that the job we do will be a much better one for having been away from it for a while.

Many people, while agreeing in general that periodic vacations are highly desirable, nevertheless maintain that this is a luxury which they must forego, for a variety of reasons. This is an unfortunate point of view, and one that would be very easily changed could they but spend a few days as an unofficial observer in any doctor's office. There they would see patient after patient, in varying stages of ill health, unable to carry on their daily tasks efficiently. Many of these patients, to be sure, have organic diseases of different types and of various grades of severity. About 50 per cent of them, however, are organically quite sound. As their stories and symptoms unfold, the doctor realizes that their headaches and faulty digestions, their backaches and dizzy spells, are the direct result of life's stresses and strains and their worries and anxieties. With this group of patients, relief will be obtained not from the contents of a medicine bottle, which they all so earnestly seek. There is only one prescription that will give these individuals relief, and that prescription cannot be filled in any drugstore. That prescription is *rest*. Not only physical rest, but what is far more important, mental rest. I do not mean to imply that a periodic vacation will automatically restore this group of individuals to good health, but it will almost certainly result in marked and immediate improvement, it is at least one very important step on the road to recovery.

But why wait until we are rundown or ill before applying the remedy? Why not far more sensibly so arrange our affairs that a vacation is taken at least once a year, thereby minimizing our chances of becoming ill? That much illness can actually be prevented by vacations is very well known to physicians. This point was amusingly

\*A. Green Lights to Health, broadcast given by Dr. Alfred Kraines on June 11, 1940 and sponsored by the Public Education Committee of the Massachusetts Medical Society and the Massachusetts Department of Public Health.

illustrated several years ago in the advice given to a group of medical students by an eminent doctor. He advised them, when they were ready to begin practicing not to start in the fall because the summer vacations so improve people's health that the young doctor relying on new patients might become very discouraged. To avoid this discouragement he advised them to start in the spring when, because of the overwork and fatigue of the winter patients would be more plentiful.

There is just one more point I should like to emphasize. Most of us, regardless of how interested we are in our work, develop a certain degree of irritability after being constantly on the job for any length of time. Petty things begin to annoy us, we snap at people for no apparent reason, and quarrels begin to arise at home where heretofore all had been peaceful. We become difficult to live with and to get along with. The effect of a vacation on this state of affairs is usually miraculous. After a change of scenery and a rest, the world usually seems like a much better place in which to live, and our dispositions are much improved.

*Q* Most of us really do not object to vacations, but the problem of expense is probably the most important single factor preventing the majority of people from taking one. Would you mind saying a little more about that?

*A* "I can't afford it" is naturally what most people say whenever the doctor advises a vacation. But you must remember that we can all afford to keep well. Unfortunately people can only see what immediately concerns them, and in the vacation problem, it is the actual amount of money that a vacation involves. What they fail to see because it is not imminent, is the cost of the illness that a vacation now and then may have prevented—not only the cost of doctors' bills and medicines, but the loss of wages that illness produces.

On the other hand, by budgeting income properly as is done in Christmas Clubs, for example, sufficient money could be saved throughout the year to give many people a vacation they can afford. All it needs is a little planning.

*Q* How long a vacation would you advise?

*A* A little longer. I am afraid than most people are able to take. The standard vacation seems to be about two weeks, and certainly two weeks out of fifty-two is the minimum that anyone ought to have. If it can possibly be done, four weeks once a year or two weeks twice a year is ideal. If two weeks is all that is available, it should be supplemented whenever possible by week ends away from our accustomed surroundings.

*Q* Do you think it makes any difference what time of the year vacations should be taken?

*A* Not the slightest. Whenever we can get the most fun and relaxation is the time to take our vacations. For many years, the summer has been the customary vacation season, but winter vacations are becoming increasingly popular. I think it will be very interesting to see whether the amount of disability due to respiratory infections during the cold months will be diminished as the winter vacation season increases.

*Q* If as you say a vacation now and then is necessary for maintaining good health, does it make any difference where we go? To put it another way is one place more healthful than another?

*A* I do not believe so. The choice of where one goes depends on individual tastes. Whether it is the mountains or seashore, the city or the farm, actually makes very little difference provided we enjoy ourselves and get into

new surroundings. A large city, for example, may not sound like a desirable vacation spot to most city dwellers but to people who live on a farm the year round, it may be an ideal place to go. So far as concerns the old controversy about the mountains being more healthful than the seashore or vice versa, there actually is nothing to it from a medical point of view. There may be occasional cases, in which for special reasons, certain places are to be preferred but for most of us my only advice is go wherever you like and where you will have the greatest pleasure with the least responsibility.

*Q* Are there any special precautions or advice that you think ought to be given to people going off on a vacation?

*A* Well it seems a bit queer to urge you in one breath to go away and enjoy yourself and in the next breath to warn you about the trouble you may get into on a vacation. Nevertheless, in order that you may get the most out of it, perhaps it might be wise to mention several precautions.

The first thing that occurs to me is the common practice of sun bathing and its dangers. I am not referring to the usual painful sunburn which may by the way, be quite serious. Although sunlight in repeated small doses may be quite beneficial, longer exposure, aside from the burn may prove quite harmful. This is especially true in old people, in whom excessive exposure to the sun may result in serious strain on the heart. In any case it does them no good, despite all that is claimed for it and contrary to popular notions. I should advise all over fifty to protect themselves from the sun.

Another point which might be stressed again is the danger of overexertion. Here also the danger is not so much to young adults as to those above forty. To switch suddenly from a job behind a desk or counter to long distance swimming or mountain climbing may be inviting serious trouble and even at best, the aches pains and fatigue following this unaccustomed effort do nothing to add to the joy of life which was the primary purpose in going on a vacation.

## DEATH

POPE—ERNEST F. POPE, M.D., of Boston died January 26. He was in his sixty-seventh year.

Dr. Pope received his degree from the University of Colorado School of Medicine in 1907, and had specialized in industrial surgery. He was a member of the Massachusetts Medical Society and the American Medical Association.

## MISCELLANY

### NOTES

It has been recently announced that the winner of the 1940 Mississippi Valley Medical Society Prize Essay is Dr. John W. Casey of Boston for his paper "The Study of the Use of Sulfapyridine and Sulfathiazole in Pneumonia, with Particular Reference to the Treatment of Pneumonia." Dr. Casey will present his essay at the sixth annual meeting of the society to be held in Rock Island, Illinois, September 25, 26 and 27.

Recent dispatches list Dr. Laurence O'Shaughnessy of London as having been killed in action while serving with the Medical Corps of the British Army. Dr. O'Shaughnessy had gained world wide fame for his operation of cardio-omentopexy, in which a portion of the omentum is brought up through the diaphragm, carried

through the pericardial sac and sutured to the heart in order to provide additional circulation in cases in which marked cardiac ischemia, due to coronary sclerosis and thrombosis, is present. He had quite recently visited the United States, and during his stay had presented a paper before the New England Heart Association

## CORRESPONDENCE

### RESTORATION OF LICENSE

*To the Editor* This is to inform you that in accordance with the vote of the Board of Registration in Medicine, the license of Dr. English N. McLaughlin, revoked on May 25, 1933, was restored on June 6, 1940

STEPHEN RUSHMORE, M.D., *Secretary*

State House,  
Boston

## REPORT OF MEETING

### WILLIAM HARVEY SOCIETY

At a regular meeting of the William Harvey Society held at the Beth Israel Hospital on April 5, Dr. Emil Novak spoke on "The Endocrine Influence of Certain Ovarian Neoplasms"

The speaker elucidated the subject on the basis of an embryological concept, recounting the normal phases of development of the germinal cells. It was hypothesized that groups of cells "ripped off" at various stages remain quiescent for some time and then become neoplastic and function according to their degree of differentiation at the time of segregation.

Tumors arising from cell rests of an early stage may occur in either the testis or ovary, they are markedly undifferentiated and have no functional activity. These are the dysgerminomas of the ovary or testis or the seminomas of the testis.

The first developmental stage is more or less toward a male phase with the female aspect being only evanescent. It is at this time that the testicular cords develop, and union with mesonephric structures occurs. Consequently, remnants of such cells later function to upset the intersexual balance in an individual toward maleness. Thus arrhenoblastomas may cause defeminization or masculinization.

As the germinal procession goes on there is a secondary wave of female development wherein the cells are grouped around the germ cells to form the future ovum and surrounding follicular epithelium. Overabundance of these cells may eventually be the cause of granulosa-cell tumors, which have the ability to produce estrogens and thus are feminizing tumors. The origin of both granulosa and thecal cells now appears to be mesenchymal in character rather than secondary to an ingrowth of germinal epithelium, so that thecomas and granulosa-cell tumors are properly part of one tumor group. This explains the usual picture of varying mixtures of the two types of cells in these tumors.

Dysgerminomas are prone to occur in those of poor sexual development, such as pseudohermaphrodites, despite their absence of sexual potentiality. Consequently, removal of these tumors has no effect on the underlying sexual balance.

Granulosa-cell cancers and thecomas both produce estrogen, and therefore have identical endocrine effects. Occasionally lutein-like cells may be formed, and if so, progesterone effects, such as postmenopausal decidual, may be

found. Naturally the endocrine effects of such tumors depend on the existing hormonal balance, thus the resultant manifestations are much more striking before puberty and after the menopause, when the amount of existing estrin is small.

In the very young, such neoplasms are a cause, although a relatively infrequent one, of precocious menstruation and development of secondary sex characteristics. The bleeding in such girls, however, is nonovulatory in contrast to that from extraovarian causes, such as small pituitary adenomas. During the reproductive phase of life, granulosa-cell cancer is one cause of menstrual disorders. There may be functional bleeding, normal menses or complete amenorrhea. The latter phenomenon is a result of continuous stimulation with estrin, a procedure which has been proved to be a means of producing amenorrhea. In the postmenopausal period there may be resumption of normal menstrual cycles with a certain amount of uterine rejuvenation, the breasts, however, do not share in this reversion. The typical manifestations of a second menopause on removal of granulosa-cell tumors in such women were offered as evidence that the pituitary stimulation which causes the symptoms of the menopause is secondary to the withdrawal of estrin.

Luteomas were considered to be luteinized granulosa-cell tumors or thecomas. They cause postmenopausal decidual changes of the uterus and have been known to exert a masculinizing effect in certain cases. An adrenal origin may explain this latter anomaly of function, since the resemblance of progesterone, the adrenal cortical hormones and the androgens is well known.

The masculinizing tumors result from an attempt to form testicular structures in varying degree. Some are undifferentiated and simulate sarcomas, while others reproduce true cell types and have marked endocrine potentialities. Arrhenoblastomas may occur at any age, but usually appear during the third decade. The early manifestations are those of defeminization, such as amenorrhea, decrease of the breast tissue and loss of the female contour. Later, masculinization in the forms of a deep voice, enlarged larynx and clitoris, and hirsutism may ensue. Removal of the tumor causes definite but varying degrees of regression, with the menses and breast development showing the earliest changes. The masculine characteristics, especially the enlargement of the clitoris, retrace their course more slowly and often incompletely.

Adrenal rests may cause the same syndrome as that of the arrhenoblastomas, a fact which is not surprising when one considers the close embryological connection of the adrenal cortex and the ovarian medulla. In suspected cases, the pelvis should be examined, and the finding of an ovarian tumor, combined with the characteristic symptoms, should be taken as presumptive evidence of its etiologic relation.

## NOTICES

### ANNOUNCEMENT

CLITO R. DAMIANI, M.D., announces the removal of his office from 13 Kingsley Street, Allston, to 142 Craft Street, Newtonville.

### UNITED STATES CIVIL SERVICE EXAMINATIONS

Chief Medical Officer \$6500 a Year

Applications must be on file with the United States Civil Service Commission at Washington, District of Columbia, not later than July 8.

Applicants must have been graduated with an M.D. degree from a medical school of recognized standing or must be a licensee of the National Board of Medical Examiners. In addition they must have had certain highly responsible professional experience in the field of medicine, partly in a managerial or supervisory capacity. Applicants obtaining the highest ratings may also be requested to appear for an oral examination.

Full information regarding the examination and the application form may be obtained from the Secretary Board of U. S. Civil Service Examiners at any first or second-class post office, or from the Civil Service Commission, Washington, District of Columbia.

## SOCIETY MEETINGS AND CONFERENCES

SEPTEMBER 2-6—American Congress of Physical Therapy. Page 662  
Issue of May 16.

OCTOBER 8-11—American Public Health Association. Page 655  
Issue of April 11.

OCTOBER 11-12—Pan-American Congress of Ophthalmology. Page 658  
Issue of May 23.

OCTOBER 14-25—1940 Graduate Fortnight of the New York Academy of Medicine. Page 938, Issue of May 30.

OCTOBER 21—American Board of Internal Medicine. Page 369  
Issue of February 29.

JANUARY 4, 1941—American Board of Obstetrics and Gynecology. Page 1064  
Issue of June 20.

APRIL 21-25, 1941—American College of Physicians. Page 1065  
Issue of June 20.

## DISTRICT MEDICAL SOCIETY

MIDDLESEX NORTH

JULY 31.

OCTOBER 30.

## BOOK REVIEWS

*A True History of the Terrible Epidemic Vulgarly Called the Throat Distemper Which Occurred in His Majesty's New England Colonies between the Years 1735 and 1740* by Ernest Caulfield, M.D. 8 half cloth 113 pp., with illustrations. New Haven Conn. published for the Beaumont Medical Club by the Yale Journal of Biology & Medicine 1939 \$2.50

Dr Caulfield will earn the gratitude of students and practitioners of medicine for this excellent, readable account of the terrible epidemic of "the throat distemper" which occurred in His Majesty's New England colonies between the years 1735 and 1740.

The author points out that, unfortunately for a scientific analysis, "the throat distemper" was a complicated epidemic, in that it consisted of a scarlet fever and two separate diphtheria epidemics. It is certain, the author continues to write, that diphtheria was endemic in the colonies for many years, particularly in Massachusetts and Connecticut, but not enough records are available to make a statement concerning its presence in New Hampshire. Scarlet fever was present certainly in Massachusetts and probably in New Hampshire, but there are no early records of it in Connecticut. The epidemic is carefully traced through towns in New Hampshire, Maine, Massachusetts and Connecticut, and reference is made to it in the states of New York and New Jersey.

One of the very noticeable characteristics of the epidemic was the occurrence of many deaths in the families of ministers and physicians. Many in seeking for a cause, were led to look beyond natural causes to the Hand of God, to whom we are chiefly concerned to apply ourselves for the Removal of this awful Calamity." In Boston, on the other hand, "a consultation of Practitioners in Physick agree upon one important point. That the said

Distemper proceeded from some occult Quality in the Air and not from any observable Infection communicated by Persons or Goods."

The student of medical history will especially appreciate the careful documentation of this book. It will be indispensable to the special student of infectious diseases.

*Gardiner's Handbook of Skin Diseases* Revised by John Kinnear T.D., M.D. M.R.C.P. (Edin.) Fourth edition 12 cloth 239 pp. with 70 illustrations and 16 colored plates. Baltimore Williams & Wilkins Company, 1939 \$3.50

This small handbook which is well printed with large readable type on good paper does not present an adequate exposition of its subjects. It is somewhat more extensive than a quiz compend, but there are many fairly common recent therapeutical procedures which are not mentioned. For instance, in psoriasis, the chrysarobin substitutes, such as anthralin are not discussed.

The colored plates which were prepared from Dufay color photographs are quite good but those which are obviously color photographs of moulages have a somewhat ancient appearance. The author's sketches indicating the histology of skin diseases are very naive and charming in their simplicity but therein lies some criticism because they barely more than indicate, somewhat vaguely the outstanding microscopic characteristics. It is a pity that more effort to make them comprehensive was not expended.

It can hardly approach its aim as a handbook for the general practitioner unless the term handbook is used in a much more restricted sense than it usually is. It might do for students who are interested in no more than a quick sketch of some dermatoses.

*Textbook of Medical Treatment by Various Authors* Edited by D. M. Dunlop B.A. (Oxon) M.D., F.R.C.P. (Edin.) L. S. P. Davidson B.A. (Camb.) M.D., F.R.C.P. (Edin.) M.R.C.P. (Lond.) and J. W. McNeer, D.S.O., D.Sc. M.D. (Glas.) F.R.C.P. (Lond.) with a foreword by A. J. Clark, B.A. (Camb.) M.D. D.P.H., F.R.C.P. (Lond.) F.R.S. 8 cloth 1127 pp., with 27 illustrations and charts and tables. Baltimore Williams & Wilkins Company 1939 \$8.00.

This is a textbook on medical treatment written by a group of Scotch physicians associated with the hospitals and schools in Edinburgh and Glasgow and bears the stamp of thoroughness and conciseness and the sense for the practical which characterize medicine in Scotland. It is a good book. It aims to consider the management of the case in the widest sense of the term and deals with therapy in its manifold applications. Furthermore the authors "make an attempt to be extremely explicit in regard to the treatment recommended in the hope that the directions given will suffice to enable a doctor without much previous experience to carry out the measures which have been described."

It is thoroughly up to date. Frequently, physiology and etiology are discussed briefly where these are essential to a thorough understanding of treatment. Diet particularly is stressed and detailed lists and instruction are given with the individual disease entities. The authors recognize that a large portion of the physician's work is in relation to functional disease, and emphasize this aspect of therapeutics.

As one becomes more acquainted with this book it stands out as one of the better of the many textbooks on treatment.

*Obstetrical Manikin Practice* By Lyle G McNeile, MD 4°, cloth, 111 pp., with 38 illustrations Baltimore Williams & Wilkins Company, 1939 \$2.00

This small volume is designed for medical students who are taking a manikin course in obstetrics. Its purposes are to acquaint its readers with the anatomy of the female pelvis and to instruct them in the mechanism of normal birth and in the indications for and the technic of operative delivery. These aims are fulfilled in a satisfactory manner. The author's description of the mechanism of labor in vertex presentations, while departing in some respects from the classic accounts in standard textbooks, is probably correct, since it is based on reliable x-ray studies. The operative maneuvers advocated are those of sound modern obstetric practice.

The book may safely be placed in the hands of students, if their instructors will delete certain references to manual dilatation of the cervix—a dangerous procedure now justly in bad repute. In particular should the erasure be especially thorough where the suggestion is made that in performing a Braxton Hicks version for placenta previa, it may be necessary to stretch the cervix sufficiently in this manner to secure a foot.

No mention is made of the increased height of the pelvis that is so often found in contractions of the male type and that is shown by lengthening of the pubotuberous diameter of Schuman. There are no illustrations of the soft parts making up the pelvic floor, which is of much more importance in the mechanism of normal labor than is the bony pelvis. In fact, since the whole book is devoted to the mechanics of normal and operative delivery and since a clear understanding of such mechanics depends on a series of accurate mental pictures in the minds of students, the illustrations might well have been increased in number.

*A Text Book of Occupational Diseases of the Skin* By Louis Schwartz, MD and Louis Tulipan, MD 8°, cloth, 799 pp., with 116 illustrations Philadelphia Lea & Febiger, 1939 \$10.00

Occupational dermatoses are assuming greater importance, and a book of this type should be a welcome addition to the library of many physicians. The subject is discussed from a general standpoint in the first 75 pages, in which are lists of substances for patch tests and a description of the methods of investigation of occupational skin diseases. Classification is discussed, and the matters of diagnosis, incidence and general methods of treatment also receive consideration.

The bulk of the book is devoted to the dermatoses caused by various agents, with many single chapters devoted to a particular substance. A large number of processes are discussed in detail, and information is provided about the risks attendant on the use of various substances. There are many valuable lists, such as cosmetic ingredients, dyes, fungicides, plants, resin plastics, woods and so forth and there is much information about the various types of infections which possibly may be received in the course of work. Another section reviews the skin hazards in many different occupations. Finally, there is a chapter with data about many known irritants, and the most important industries in which they are employed. Thus the agent or the occupation may be reviewed by the physician.

There are numerous illustrations, and an excellent index. The book as a whole is well done and will be a valuable reference book for physicians doing part time or full time industrial work.

*Recent Advances in Medical Science A study of their social and economic implications* A Rede Lecture delivered before the University of Cambridge, on April 28, 1939 By Sir Edward Mellanby, KCB, MD, FRCP, FRS. KHP 12°, paper, 62 pp. Cambridge, England At the University Press, 1939 \$75

In a very brief report, given as one of the Rede Lecture at the University of Cambridge, Sir Edward Mellanby the energetic secretary of the Medical Research Council has summed up some of the recent advances in medical science. The account is an extremely readable one but loses a good deal on account of its brevity.

*Practical Obstetrics* By P Brooke Bland, MD and Thaddeus L Montgomery, MD Third revised edition. 4° cloth, 877 pp., with 502 illustrations, including 27 colored plates Philadelphia F A Davis Company, 1939 \$8.00

This textbook, which is in reality a new edition of Bland's volume with Montgomery as co-author, is clearly and systematically written and adequately illustrated. Since it covers the subject in a rather cursory manner, it is more suited to students beginning their study of obstetrics than it is to practitioners seeking detailed information. It has two weaknesses. The section on obstetric pathology is considerably out of date, showing no change from the edition of Bland's book which was published in 1932. It is doubtful if the description of the pathological picture in pernicious vomiting or in eclampsia is sufficiently accurate to be acceptable today. The account of the medical and surgical complications of pregnancy does not appear adequate in view of the great amount of attention that these matters are now receiving.

*Nutrition and Diet in Health and Disease* By James S McLester, MD Third edition, entirely rewritten. 8° cloth, 838 pp., with tables Philadelphia and London W B Saunders Company, 1939 \$8.00

There is no denying the fact that one of the fields of medical science which has attracted widespread attention is that of nutrition. Indeed, the advances which have been made in the past few years are so numerous that it is difficult for anyone to keep fully informed. With the appearance of the third edition of Dr McLester's book there is now available, in one volume, the information that every physician is anxious to obtain readily. This book has been entirely rewritten, and it is refreshing to find discussions of disordered physiology in preparing the reader for the outlines of the dietary treatment of disease. The material is clearly presented, and the text can be read with ease. This third edition should enjoy the same popularity as the first and second, and every well informed physician will want to own a copy.

*Historical Directory of State Health Departments in the United States of America* By Robert G Paterson, PhD 8°, paper, 68 pp. Columbus The Ohio Public Health Association, 1939 \$1.00

The author has compiled a useful manual giving the name of the current executive in each state health department, with the names and titles of all executives since the establishment of the department. There is also a very valuable bibliography of all reports and publications of the various health departments. It is interesting to note that the Massachusetts Department of Public Health, established in 1869, was the first of its kind in the United States.

# The New England Journal of Medicine

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VOLUME 223

JULY 11, 1940

NUMBER 2

## CESAREAN SECTION IN MASSACHUSETTS IN 1938\*

ROBERT L. DeNORMANDIE, M.D.

BOSTON

WHEN the Executive Committee of the Section on Obstetrics and Gynecology<sup>1</sup> reported at the annual meeting of the Massachusetts Medical Society in 1938 on the cesarean sections for 1937, we did not know that we should be asked to continue the study. Since that time the Massachusetts Department of Public Health has asked us to make this a five year study. This report therefore, is for the second year, 1938. Although

In Massachusetts in 1938 there were 62,382 live births and 1730 stillbirths, a total of 64,112. Of these, 50,888 were reported to us as occurring in hospitals. There were 2216 cesarean sections performed and 16 hysterotomies, a total of 2232 abdominal deliveries or an incidence of 1 in 287. Table 1 gives a summary of the abdominal deliveries.

Table 2 gives the indications for the 16 hysterotomies. Serious cardiac disease was responsible

TABLE 1. Summary of Abdominal Deliveries

Operation	N	C. 381
Cesarean section	2216	
Emergency	995	
Elective	1196	
Not reported	25	
Type of operation		
Low	1406	
Classical	914	
Latzko	14	
Porro	5	
Peritoneal exclusion	1	
Not reported	37	
In labor	744	
Not in labor	1491	
Not reported	39	
Membranes ruptured	331	
Membranes unruptured	1867	
Not reported	78	
Hysterotomy	16	
Total	2232	

TABLE 2. Indications for Hysterotomy

Indication	No. of Cases
Cardiac disease	
Hypertension	2
Multiple sclerosis	1
Hydriform mole	1
Tuberculosis	1
Erythroblastosis in previous pregnancy	1
Pelvic stenosis	1
Manic depressive insanity	1
Total	16

members of the committee have examined the figures, I alone am responsible for the opinions expressed. The same questionnaire was used for this report as was used in the first year. The report follows closely that for 1937, in order that comparisons may be readily made.

The questionnaire was sent to 171 licensed maternity hospitals. Replies were received from all thirty-eight hospitals reported no cesarean sections for the year. These were all small hospitals not equipped to do such operations.

It is interesting to note that 2 hysterotomies were done because of the presence of multiple sclerosis, and in the analysis of indications for cesarean section (Table 5), 3 were done for the same disease. The single case of erythroblastosis in a previous pregnancy as an indication for hysterotomy needs explanation. It is a recognized fact that it recurs in about 80 per cent of pregnancies. This patient had previously had an erythroblastosis of the icterus gravis type, and following a consultation it was thought best to sterilize her. Therefore a hysterotomy with sterilization was done. The other indications need no comment.

Table 3 shows the types of anesthesia employed. As in the first report, nitrous oxide oxygen and ether was by far the commonest anesthetic. The use of cyclopropane and spinal anesthesia has increased. Anesthesia was recorded

\*Presented in abstract before the Obstetrical Society of Boston, November 21, 1939.



as the cause of death in 5 cases, all elective sections They are reported below

Table 4 shows the recorded indications for operation in the cases in which the babies died There

TABLE 3 *Types of Anesthesia*

ANESTHETIC	No. OF CASES
Nitrous oxide oxygen and ether	1533
Ether	260
Cyclopropane	159
Spinal	106
Nitrous oxide and oxygen	19
Avertin	29
Local	34
Other	50
Not reported	26
Total	2216

were 131 emergency cesarean sections in which the baby was lost, and 55 elective operations, with the loss of 56 babies, including one set of twins

Why should 27 babies have been lost in elective cesarean sections done because of previous sections? Analysis of these deaths brings out some interesting points In 6 cases the cause of death was recorded as prematurity In 6 others it was pulmonary atelectasis Were these patients oper-

TABLE 4 *Indications for Operation in Cases with Death of the Baby*

INDICATION	EMERGENCY CESAREAN SECTION	ELECTIVE CESAREAN SECTION
Separated placenta	45	—
Placenta previa	29	2
Toxemia and nephritis	14	7
Previous cesarean section	7	27
Prolonged labor	12	—
Contracted pelvis	5	6
Ruptured uterus	6	—
Previous operative attempts	3	—
Desire of patient	—	3
Eclampsia	2	—
Test of labor	2	—
Previous disaster	—	2
Prolapsed cord	1	—
Double uterus	1	—
No progress	1	—
Multiparity	1	—
Cervical dystocia	1	—
Hydrocephalus	—	1
Previous vaginal operation	—	1
Ankylosis of hip	—	1
Advanced age and rigidity of cervix	—	1
Pyelitis	—	1
Chorea	—	1
Brain tumor	—	1
Thyrototoxicosis	—	1
Not reported	1	1
Totals	131	56

ated on too early? Was too much medication given the mother before operation? Six other babies were recorded as stillborn with no explanation Three of them, however, were macerated, and 1 of these was an anencephalic infant There were 2 monstrosities, 1 baby with congenital absence of the bile ducts and 1 with erythroblastosis These last two conditions, of course, were totally unpredictable One baby died of inanition

in four weeks' time, and in 1 resuscitation failed One each died of purpura of the newborn, intra cranial hemorrhage and bronchopneumonia

That 13 babies should be lost through prematurity and inability to establish respiration is a serious criticism One of the reasons for doing a section on toxemic cases is to obtain a living baby, yet in 7 elective sections the baby was lost That the babies were lost in 3 elective cesarean sections done because of the desire of the patient, is shocking It is also inexcusable that 2 babies should have died after cesarean section done because of previous disasters, and it is hard to explain why 6 babies were lost when the indication was a contracted pelvis

The other indications would be questionable if living babies had been obtained, but with the loss of the babies they are without justification

In the emergency cases, it is not surprising that 45 babies died because of separated placenta The percentage, 44 per cent, is to be expected with this complication The question arises whether some of these mothers would not have been better delivered from below than by cesarean section It is easy to understand why babies were lost following prolonged labor, ruptured uteri and previous operative attempts Little need be said in regard to the deaths of babies in the other emergency sections In some cases severe criticism is due the physician for choosing a section as the method of delivery

Table 5 records the indications for cesarean section As last year, the indications were various and bizarre With the number of cesarean sections that are being done in Massachusetts, it is of course reasonable to have the indication of previous section lead the list The next most frequent indication is disproportion How many of these cases presented a disproportion sufficient to warrant a section, it is impossible to judge However, one gets the impression that many sections done for this indication were unnecessary

The number of cesarean sections done for separated placenta has increased decidedly It is doubtful whether all were justified, for several patients were only six or seven months pregnant and undoubtedly could have been managed better from below, by rupturing the membranes and using the Spanish windlass

The number of sections for toxemia and nephritis remains about the same Were ideal prenatal care given all patients, undoubtedly the incidence would be lower That it should seem essential to do 125 sections for these conditions shows a total lack of co-operation on the part of the patient and of careful, intelligent treatment by the physician

Malposition of the baby as an indication needs little comment, except that it seems that cesarean section is done with increasing frequency for breech presentations.

Under the grouping 'Dystocia' there were 202 cases. There has apparently been a greater attempt

explanation. The criterion for decision in regard to previous myomectomies, I think, is the size, position and number of scars in the uterine wall. As these are unknown, the indication must be accepted as valid. In the case of a previous gastro-enterostomy, it was thought that a section would

TABLE 5 *Indications for Cesarean Section*

INDICATION	NO. OF CASES	INDICATION	NO. OF CASES
Previous section	435	Elderly primipara	70
Contracted pelvis and disproportion	477	Obstructing tumors (fibroids)	18
Placenta previa	15	Fetal distress	7
Separated placenta	104	Prolapsed cord	3
Toxemia and nephritis	125	Following operative attempt	7
Eclampsia	9	By request or for sterilization	17
Malposition of baby	110	Request	6
Breech	8	Sterilization	11
Transverse	22	Ruptured uterus	8
Brow	1	Spontaneous	1
Shoulder	2	Previous section	7
Face	5	Injury or disease of pelvis	6
Prolapse of hand	1	Bicornate uterus	3
Compound malposition	1	Postmaturity	4
Dystocia	202	Social and economic reasons	3
Dystocia	28	Varicose veins of vagina	1
Labor without progress	47	Congenital dislocation of femur	1
Tent of labor	60	Malformation of fetus	1
Cervical dystocia	30	Abdominal hernia	1
Uterine inertia	6	Obesity	1
Persistent ODP	1	Malformation of vagina	1
Contraction ring	1	Desire for live baby	1
Previous surgical operations	43	Frequent miscarriages	1
Repair of perineum	4	Bizarre	25
Amputation of cervix	6	Twins—3 with locked heads	5
Repair of cervix	3	Pa right hip	1
Suspension of uterus	4	From history of caesarean section	1
Myomectomy	1	Elderly multipara	1
Vaginal operations	1	Multiparity	1
Gastroenterostomy	1	High nervous state of mother	1
Thyroidectomy (5 months before)	1	Fetal dystocia	1
Nephrectomy	2	Teliofibrosis (fatal caesarean section)	1
Associated medical conditions	61	Thickened placenta previa	1
Cardiac disease	31	Maternal debility	1
Tuberculosis	5	Wentworth-Hicks contractions	1
Diabetes	9	Pregnancy at term	4
Bronchiectasis	1	Unengaged head	1
Epilepsy	1	Impure of membranes and no labor	1
Chorea	1	Length of ruptured membranes	1
Faginus ossificans	3	Right occiput (transverse by a 2)	1
Multiple sclerosis	2	Not reported	48
Psychosis	2		2.16
Arthritis	2		
Pylori	2		
Brain tumor	1		
Hypothyroidism	1		
Previous obstetric disaster	47	Total	

to allow a test of labor than appeared from the first report. Whether or not this is simply a slight change in the way the questionnaires were answered, it is difficult to say. Sixty sections were done for cervical dystocia and uterine inertia, but when it appears that patient after patient had only a few hours of labor, often reported as mild or poor, one cannot help wondering whether all these sections were necessary.

It is impossible to evaluate accurately the next group of cases, 'Previous surgical operations.' It is, however, fair to make a few comments. A simple repair of the perineum or of the cervix cannot all ways be said to be an adequate indication, while after amputation of the cervix section is the conservative procedure. Suspension of the uterus should seldom call for a subsequent section.

The other indications under this group need little

be the best way out of a serious complication. The justification for a section because of a goner operation five months before term is probably questionable. In the nephrectomy cases both patients showed severe toxemia.

Under 'Associated medical conditions,' cardiac disease leads the list. There is no way of judging whether all the cases should have had sections. Many cardiac patients, especially multiparas, have a surprisingly easy labor, and there is not the risk of distention that might follow a section.

This year it happened that 9 diabetic patients had sections. The explanation is that these women were under the care of physicians who believed that many such cases are better managed by a section than by allowing the patient to go through labor. There are in Boston two totally different schools of thought in the management of diabetic cases.

Previous obstetric disaster may or may not be a proper indication. Each case of this type must be carefully studied and the decision must depend on the individual case. The mere fact that a woman has had one disaster is not an absolute indication for a cesarean section in the next pregnancy. Again, the fact that the patient happens to be an elderly primigravida is not in itself an indication for a section. Each case requires individual study before a reasonable and sane decision can be made.

A cesarean section done because of fetal distress resulting in a stillborn baby is a dubious procedure. It is equally questionable to do one because of fetal distress, and have the baby cry just as it is being born.

Subjecting a woman to a cesarean section because of a prolapsed cord undoubtedly is justifiable in

the pelvis has been so narrowed that a delivery cannot be safely accomplished.

I have grouped as bizarre indications those given for 25 sections. Others could readily be placed in this group. There is no need to comment on each of these. It is apparent to any thoughtful observer that they are not good and sound reasons for subjecting a woman to a major operation.

In 1938 there were, as I have already reported, 2232 abdominal deliveries with 60 maternal deaths, giving a maternal mortality rate of 2.7 per cent. This is an excellent result, a little lower than that of 1937, which was 3.1 per cent.

No comment need be made on Table 6, as it is simply an analysis of the operations where death of the patient followed.

In Figures 1 and 2, the data are presented in a different manner from similar data in the first re-

TABLE 6 Summary of 60 Cases with Maternal Death		
DATA	NO. OF CASES	
Emergency operation	39	
Elective operation	21	
Not reported	0	
Type of operation		
Low	26	
Classical	24	
Porro	3	
Through rupture	2	
Not reported	5	
In labor	25	
Not in labor	30	
Not reported	5	
Membranes ruptured	18	
Membranes unruptured	37	
Not reported	5	
Babies		
Living	43	
Dead	17	

some cases, but the decision requires careful judgment.

The seriousness of doing a section after operative attempts is shown by the fact that of the 7 cases in which that indication was given, 4 mothers and 4 babies were lost.

I cannot bring myself to accept the request of the patient as a reasonable indication for a section. Nor do I believe that cesarean section for the purpose of sterilization is good practice. In my opinion it is much safer to allow the patient to have a normal delivery, and if sterilization is indicated to do it at a later time.

Of the 8 cases of ruptured uterus, 1 was spontaneous and 7 were the result of previous cesarean sections. That, of course, is what we must expect with the increasing incidence of cesarean section.

It is understandable that there might be so severe an injury to or disease of the pelvic bones that a cesarean section would be indicated. But the fact that the patient has had such an injury is not itself an indication for one. The criterion is whether

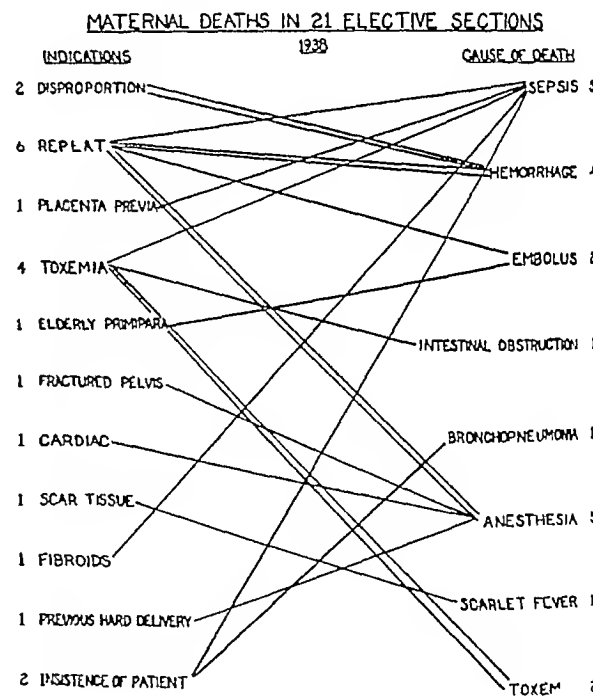


FIGURE 1

port. They show more clearly the indications for operation and the causes of death in the 60 cases with fatal results. Figure 1 analyzes the 21 elective sections and Figure 2 the 39 emergency operations in which death occurred. I have already spoken of many of the indications, and there is no need of making further comment on these. But the causes of death in the 21 elective sections must be analyzed.

That 5 patients died of sepsis makes it clear that obstetricians and surgeons must be more careful in their operative technic. The same is true of hemorrhage. There should not have been 4 deaths

from this cause. The 2 deaths from pulmonary embolus cannot be regarded as preventable. In the death that took place from intestinal obstruction, the patient was operated on three days after the original operation, and the obstruction was freed, but she failed to survive the second operation.

Whether the death from bronchopneumonia can be considered an anesthetic death is question

garded as preventable. The 2 deaths from toxemia show that there had been inefficient prenatal care, and the choice of cesarean section was unwise.

Figure 2, which gives the indications and causes of death in the 39 emergency sections, demonstrates the seriousness of doing emergency sections in cases not properly prepared. Seventeen of these women died from sepsis. It is not necessary to mention each indication, but it should be noted that of the 5 patients whose labor was prolonged 4 died of sepsis. There were 4 deaths following previous operative attempts, 3 from sepsis and 1 from shock, the patient not living long enough to develop sepsis.

Again this year we have deaths from anaphylaxis. This suggests that the technic in the matching of blood must be perfect, or serious reactions with death will follow.

The patient who died of acute pulmonary edema was badly managed outside the hospital, and she was in very poor condition on entrance. In spite of proper treatment after entrance, death followed.

Whether the cases classed under premature separation are correctly assigned is uncertain. There was, however, no marked hemorrhage. There was not enough evidence to assign the cause to toxic separation, so I have left the cause of death as given. The number of cases of eclampsia is again low, as already reported but 1 woman died.

The last case, one of intestinal obstruction, had an emergency operation for a primiparous breech. The patient had marked distention and a rise in temperature immediately after the operation. The death certificate gave mesenteric thrombosis with intestinal obstruction as the cause of death. Whether this is correct or whether the cause was sepsis, there is no way of telling, as there was no autopsy.

In analyzing these deaths both elective and emergency, it is fair to say that the number of deaths from sepsis should have been lower. There were other obviously preventable deaths. Exactly how many, it is difficult to say. The fact that deaths from anaphylaxis and from poorly administered anesthesia are still occurring is a serious criticism of the profession. These deaths must be eliminated.

This year we have made no attempt to appraise the number of consultations that were held for the questionnaires were vague and gave us no basis on which to work. I repeat what I said in my first report. I am confident that if the American College of Surgeons should withhold its approval from hospitals where no obstetric consultations are held, the number of cesarean sections would be materially diminished.

There are, however, 5 deaths that were attributed to anesthesia. One patient, while she was going under ether, had a severe choking spell, followed by massive collapse of the lung and death. In the second case a spinal anesthetic was used. The patient died at once, and the autopsy showed that there was some cardiac complication. Whether or this is a true anesthetic death is debatable. The third case was that of a woman who had had severe attacks of asthma and had great difficulty in the first stage of anesthesia. This, I think, can be definitely regarded as death from anesthesia. In the fourth case again there was difficulty in giving the anesthetic and the patient died before the operation was completed. The last case was similar. There was considerable difficulty in the induction of anesthesia, and in twenty-four hours the patient developed pneumonia. In this case, even though the anesthesia went badly, the operation was prolonged in order to do a sterilization and an appendectomy. It would seem poor judgment to subject the patient to so much operative work when the anesthesia was going badly.

The death from scarlet fever can hardly be re-

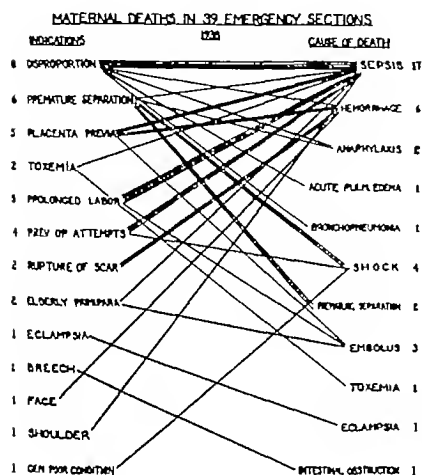


FIGURE 2.

The results from these cesarean sections throughout the State are excellent. But too many are being done, and the deaths from them are unquestionably a factor in the maternal mortality rate for the State. Cesarean sections figured in something over 20 per cent of all maternal deaths. It should be the aim of all physicians to reduce the number of unneces-

sary cesarean sections, thereby eliminating some of the preventable maternal deaths and lowering the maternal death rate.

330 Dartmouth Street

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## HIATUS HERNIA SIMULATING CARDIAC INFARCTION\*

### Report of a Case

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**H**ERNIA of the stomach through the esophageal opening in the diaphragm may be asymptomatic or may simulate a variety of other conditions, one of which is cardiac infarction. Examination of recent textbooks discloses that hiatus hernia is given scant description, or none at all. The delay and confusion in achieving the correct diagnosis have prompted the report of a case of hiatus hernia, a review of the recent literature, a description of the symptoms and an analysis of a group of patients diagnosed at the Massachusetts Memorial Hospitals.

### CASE REPORT

The patient was a 52-year-old physician, whose chief complaint was pain under the sternum and in the left arm, which woke him at 3 a.m. on December 8, 1937. He was seen by a cardiologist 5 hours later.

The pain was persistent and not completely abolished by two ¼ gr. doses of morphine. Occasional pain, of moderate severity, was noted at the inner aspect of each elbow and in the little finger of each hand. The left-sided pain predominated and the arm pains were estimated to last for 1 to 3 minutes at a time. The patient recognized little if any pressure symptoms and did not feel particularly ill. Gastric symptoms were absent.

During the subsequent 4 days he remained in bed. The white-cell count remained normal, fever was absent, electrocardiograms were normal, and the examination of the heart gave normal findings. The substernal discomfort was localized under the lower third of the sternum, where it persisted in a mild form. The patient was discharged at the end of 4 days as not having cardiac infarction but with something wrong in the mechanics of the chest.

The patient did not feel well during subsequent weeks. The above symptoms persisted in a mild form, and occasionally, in association with nervous tension, pain at the point of the left elbow reappeared and persisted for 3 to 15 minutes. The patient reported a sensation similar to that felt when one swallows something too hot. A roentgen

examination, which unfortunately did not include search for a hiatus hernia, disclosed nothing abnormal in the esophagus and gastrointestinal tract.

A vacation of 6 weeks in Florida was prescribed. He was able to play golf, but there was only slight lessening of the thoracic and arm pain. In April, 1938, the patient consulted an orthopedic surgeon who previously had successfully treated him for certain postural defects. Delay in consulting an orthopedist was in part due to the fact that the patient wished to become more certain that coronary disease was not present. The orthopedist thought that if the substernal pain was not due to cardiac disease, it could be explained on the basis of muscular strain from faulty posture. Exercises were prescribed. These were faithfully followed until September without relief of the symptoms.

On June 19 an attack similar to that of the previous December occurred. A different cardiologist was called and he, after 2 days' study of the patient as a bed case, was satisfied that cardiac infarction was not present. The symptoms were believed to be partly orthopedic, partly cardiac and partly gastric in origin.

During the summer the patient resumed active exercise without untoward symptoms. Such exertions as running an eighth of a mile, baseball and tennis for several hours did not induce symptoms. The substernal and arm pains were present with increasing frequency at other times. Finally it was noted that the pain was tending to center under the lower third of the sternum and that the raising of gas and feeling of discomfort after meals were becoming more frequent. Smoking was reduced, and omitted entirely for periods of 2 or 3 weeks. The patient thought that a gastric disturbance might be present, but obtained no relief by the taking of alkalis or the ingestion of milk, crackers and so forth. A weekly diary of the symptoms made it apparent that they were increasing in frequency, but so variable in character that their causation remained obscure. It was noted that within a few moments of going to bed the substernal and occasionally the arm pain reappeared. For lack of a better explanation the patient was forced to consider his condition a functional neurosis, although he suspected that "undiagnosed" was a possibility.

It was decided to consult a gastroenterologist. Accordingly, Dr. Chester M. Jones, of Boston, was consulted in September, 1938. He suggested the diagnosis of a small hernia of the stomach at the esophageal hiatus of the diaphragm. The hernia was demonstrated both fluoroscopically and on a roentgen plate.

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The establishment of the diagnosis was of decided value to the morale of the patient. Medical treatment for some months was of uncertain benefit. In May 1939 he consulted Dr Stuart W. Harrington, of the Mayo Clinic regarding surgical repair of the hernia. The hernia at this time could not be detected radiographically but esophagoscopic examination disclosed reddening of the mucosa of the lower end of the esophagus and a few erosions on the gastric side of the esophagogastric junction. Dilation of the esophagus was performed. Radical cure by surgery was deemed unwarranted. The patient concurred with Dr Harrington's judgment. There was a gradual abatement of symptoms to the date of writing January 1940 whatever symptoms occurred were minor and readily ignored. No treatment was followed save greater regularity in mealtime, and avoidance of large meals exertion that put pressure on the abdomen, and nervous tension.

#### RECENT LITERATURE

Hernia of the stomach at the esophageal hiatus is described mostly in the surgical literature. Among the articles are those of Moersch,<sup>1</sup> reporting 246 cases, Harrington, 416 cases, and Morton,<sup>2</sup> 46 cases among 56 patients with all types of diaphragmatic hernia. Unfortunately, information pertaining to herniation at the esophageal opening is often mixed in with that concerning other types of diaphragmatic hernia, and the latter, often larger and more spectacular, are given the fuller description of the two.

The strictly medical literature contains but little mention of the hiatus type of hernia and its simulation of coronary disease.<sup>4</sup> A good description, however, is among the recent additions to *Nelson's New Loose Leaf Medicine*<sup>5</sup>; it credits Friedenwald and Felderman in 1925 with the first description of hiatus hernia and its mode of detection. Herrick<sup>4</sup> mentions a case in which he finally demonstrated that an esophageal hiatus hernia was present, but states somewhat facetiously that the patient, a physician, still prefers his own original diagnosis of coronary disease. Perhaps this conveys a suggestion that the simulation of coronary disease by hiatus hernia of the diaphragm is often foreign to medical thinking.

#### FREQUENCY AND SYMPTOMATOLOGY

French<sup>6</sup> states that hiatus hernia is a very rare condition. However, its more frequent occurrence seems probable from the literature cited above, and particularly from Harrington's<sup>2</sup> report of 416 cases diagnosed at the Mayo Clinic. The first case in this group was demonstrated at operation in 1908; the first to be diagnosed roentgenologically was encountered in 1921. From 1908 to 1926 there were 17 such cases; from 1927 to 1938 the number rose to 399. Only 1 case was diagnosed roent-

genologically in 1927, as contrasted with 92 in 1937. Although hiatus hernias are considered to be congenital in origin, the average age at which patients in this series experienced symptoms which caused them to consult physicians was in the decade of fifty to fifty nine.

Some of the salient points, found mostly in Harrington's comprehensive article, may profitably be repeated here. The symptoms vary from none to complete disability. Although their severity tends to correspond to the size of the hernia it has been found that many small hernias cause severe symptoms.

Hiatus hernia has been termed the "masquerader of the upper abdomen." An average of three erroneous clinical diagnoses in each case in the series preceded the final recognition of the hernia. Harrington lists these in the order of their frequency as cholecystitis, cholelithiasis, gastric ulcer, duodenal ulcer, hyperacidity, secondary anemia, cardiac disease, carcinoma of the cardia, stricture of the esophagus, appendicitis and intestinal obstruction. Twenty-one patients had been subjected to operation for other conditions without benefit, but were promptly relieved when the hernia was repaired.

The chief symptoms are pain, gaseous eructation, vomiting, dyspnea, hemorrhage, weakness, anemia and cardiac palpitation. They are usually mild at first. The first symptom is often pain projected through to the back during or shortly after a meal. This pain may follow the ingestion of any substance, even a cup of coffee, into an empty stomach. It is relieved by belching or vomiting. The pain is felt more on the left side of the back and often between the scapulas. It is frequently associated with phrenic pain and may radiate down the left arm, as in coronary disease.

The pain may be worse on lying down and the patient may find relief by resuming an upright posture. The pain varies in duration from a few minutes to several hours. It shows no constant relation to physical exertion. There may be intermissions of weeks or months between attacks. When the distress has become constant, the stomach is usually found to be fixed above the diaphragm by adhesions.

A loss of weight from the reduction of food intake due to "food fear" may occur. It has also been noted that the taking of a restricted amount of food at frequent intervals, under the erroneous diagnosis of gastric ulcer, may lessen the symptoms. Hemorrhage is uncommon but gastritis

and even an ulceration in the herniated portion of the stomach have been found

Assuming an upright posture may cause the hernia to be reduced. It is for this reason that the technic of roentgen-ray examination for the detection of such hernias requires that the patient be examined in the horizontal and even the Trendelenburg position before the presence of a hiatus hernia can be excluded. It is advantageous in suitable cases to exert upward pressure by palpation deep in the epigastrium during fluoroscopic study. The use of barium is, of course, part of the technic.

#### MASSACHUSETTS MEMORIAL HOSPITALS CASES

Twelve patients seen in this hospital from 1931 to 1937 were found to have hiatus hernia.\* The hernia was demonstrated in 1 case during a laparotomy and in the others by roentgen examination. The average age was fifty-eight, and the age range forty-three to seventy-six.

None of these cases were diagnosed correctly prior to admission, and their records contain little evidence that a correct clinical diagnosis preceded the finding of the hiatus hernia during roentgen-ray examination of the stomach. One patient had apparently been diagnosed erroneously, at the time of a prior admission to another Boston hospital, as suffering from cardiac infarction.

The duration of the symptoms believed to be due to the hernia was four months in 2 cases and varied from one to ten years in the remaining 10. Pain was the outstanding symptom, occurring in 9 cases, in 5 the symptoms resembled those of coronary disease, while in 7 they suggested gastric disease.

The relation to posture was very definite in 4 cases. This means that the symptoms were prone to occur or to increase when the patient lay down.

This group of patients complained of a multiplicity of symptoms such as were described by Harrington<sup>2</sup> and in the preceding case report.

#### DISCUSSION

The case history given above illustrates a much-delayed diagnosis, a hiatus hernia was not thought of by the patient and the group of physicians consulted. I did recall an obscure case reported by Levine<sup>7</sup> in which an ulcer of the esophagus was

finally disclosed as the cause of a simulation of angina pectoris. Roentgen-ray study in January, 1938, however, disclosed nothing abnormal in the esophagus, it was not realized at the time that normal roentgen-ray findings do not exclude esophagitis. The significance of the increase in symptoms on assuming the recumbent posture was appreciated only subsequent to the diagnosis of hiatus hernia.

There is a difference of opinion regarding the need for surgical intervention. Crushing of the phrenic nerve, judging from reports in the literature,<sup>8</sup> is of doubtful value. Medical treatment may sufficiently relieve some patients whose hernias appear to cause symptoms, if not, radical repair warrants consideration. Description of the operation discloses that it is a major surgical procedure. Harrington selected 102 of his 416 cases of hiatus hernia for surgical repair, and the results were highly successful.

#### SUMMARY AND CONCLUSIONS

A case report of a patient with an esophageal hiatus hernia of the diaphragm is presented. Coronary thrombosis was simulated, and the correct diagnosis was much delayed.

A brief review of the recent literature and a description of the symptoms are offered.

A group of cases diagnosed at the Massachusetts Memorial Hospitals is included.

Hiatus hernia may simulate cardiac infarction as well as a group of gastric and abdominal diseases.

Hiatus hernia should become a more frequent diagnostic possibility in the differential diagnosis of certain cardiac and upper-abdominal diseases.

36 Hyde Avenue

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\*A larger number appear in the records of the Roentgen Department.

## A LARGE ADENOFIBROMA OF THE BREAST

## Report of a Case

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A TUMOR of the breast allowed to grow until it weighs nearly 25 pounds is a curiosity. The purpose of this paper is to describe a case of an adenofibroma of the breast which weighed 24.6 pounds (11.2 kilograms). This is the largest tumor of this type that has been reported with a pathological description and a photomicrograph. Cheate and Cutler<sup>1</sup> in their monograph on tumors of the breast mention only one fibroadenoma of the breast larger than this. It was reported by Gross and weighed 29 pounds. A perusal of the 25 articles published since 1930 that mention large breast tumors reveals very few of comparable size.

The tumor of the breast most likely to grow to tremendous proportions is the giant intracanalicular myxoma. This condition has been thoroughly reviewed by Lee and Pack,<sup>2</sup> who analyzed 109 cases. The average weight was 7.6 pounds. The only reference to extremely large tumors is von Graefes in 1838 of one weighing 22.5 pounds, Desplats's report of one measuring 40 by 40 cm and Ribbert's remark that such tumors may weigh as much as 20 kilograms. Martin<sup>3</sup> reported a breast tumor in 1933 in a sixteen year-old Negress which weighed 33.3 pounds. The microscopic examination showed diffuse myxomatous degeneration and the diagnosis was giant lipofibromyxoma, so that Martin's case belongs in the myxoma group.

Only one extremely large fibroadenoma has been reported during the last decade. MacKenzie,<sup>4</sup> of Auckland, New Zealand, mentions a thirty four year-old woman with a breast tumor of two years duration with ulceration of three weeks duration and weighing 35 pounds. The diagnosis was fibroadenoma, but no microscopical description is given. Crile<sup>5</sup> discusses large bilateral adenofibromas of the breast and reports a thirteen year-old girl with a tumor of the left breast that weighed 8.0 pounds (3.65 kilograms) and one of the right that weighed 4.7 pounds (2.12 kilograms). He states that the largest fibroadenomatous hypertrophy of the female breast that he found in the literature was that of Touraine and Renault.<sup>6</sup> This was a bilateral tumor consisting mostly of fat. The maximum circumference was 54 cm and the combined weight of both breasts was 20.1 pounds (9.15 kilograms).

## CASE REPORT

C. F. S. (No. 1344), a 52 year-old woman was admitted to the Cancer Section Westfield State Sanatorium. She had first noticed a lump in the right breast 7 years previously. At that time she consulted a physician, who advised observation. The tumor had steadily grown. Three months previously the breast had started to ulcerate. She saw a physician 2 days before admission and was immediately referred to the hospital. She gave as her reason for the 7 years delay that she feared the growth might be a cancer. The past history was irrelevant. The menopause had occurred 1 year previously. The patient had had one child but had not nursed it.

Examination was essentially negative except for the large



FIGURE 1

right breast, which measured 35 by 30 by 28 cm. (Fig. 1). It was firm and irregularly nodular. There were several ulcerations, chiefly on the lateral and posterior portions, measuring up to 6 cm. in diameter. There were no enlarged axillary nodes. Biopsy of an ulcerated area showed adenofibroma. The blood pressure was 152/72. The significant laboratory findings were as follows: urinary albumin + red-cell count 4,040,000 white-cell count 19,900 hemoglobin 81 per cent sedimentation rate 124 mm. per hour (uncorrected Westergren) nonprotein nitrogen 31 mg. per 100 cc. serum albumin-globulin ratio 0.9:1.0 total protein 6.2 gm. per 100 cc. X-ray films of the chest, skull spine, pelvis and upper femurs were negative except for arthritis of the hip joints.

A simple mastectomy was performed on the 4th day under nitrous oxide oxygen and ether anesthesia. The ulcerated areas were painted with collodion and covered with gauze. The tumor gave the gross appearance of invading the pectoralis major muscle, so a portion of the muscle was removed. There was also an extension of tumor beneath the upper portion of this muscle. A frozen section showed no evidence of malignant disease. A trans-

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fusion of 500 cc. of citrated blood was given after completion of the operation. Convalescence was uneventful.

The pathological examination was made by Dr. Robert Fienberg, who reported as follows:

**Gross Examination** The breast is greatly enlarged and nodular, forming a mass weighing 11.16 kilograms and measuring 40 by 30 by 20 cm. Ulcers are present in the skin, measuring 2.0 to 6.0 cm in diameter, the largest being necrotic, black and malodorous. Dilat-



FIGURE 2

ed veins run through the skin. The inferior surface of the dissection is lobulated, yellowish red and partly encapsulated by thick fibrous tissue. Masses of striated muscle are attached to this inferior surface and are partly incorporated in the fibrous tissue, thus giving the appearance of invasion of the striated muscle by the neoplasm. The sectioned surface of the breast reveals almost complete replacement by a huge edematous,

encapsulated, lobulated neoplasm with only remnants of compressed breast at the periphery. The lobulations are of varied size and divided by thin strands of fibrous tissue. The neoplasm is grayish yellow, with large regions of reddish brown necrosis.

**Microscopic Examination** The neoplasm consists of acini of various sizes lined by simple and pseudostratified cuboidal to columnar cells. There are a few papillary structures in wide acini and occasional mitotic figures in the epithelial cells (Fig. 2). The stroma about most of the acini is myxomatous, with dense connective tissue beyond the myxomatous region. The cellularity of the stroma varies moderately. The presence of mitotic figures indicates that the tumor was actively growing and suggests that it was still under hormonal influence in spite of the reported menopause one year previously.

**Diagnosis** adenofibroma

### SUMMARY

A case of adenofibroma of the breast weighing nearly 25 pounds (11.16 kilograms) is reported. This is the largest adenofibroma of the breast that has been reported with pathological description and a photomicrograph.

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## THE TREATMENT OF APPENDICITIS AT THE BURBANK HOSPITAL, FITCHBURG, MASSACHUSETTS\*

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**T**HREE years ago an outline of principles for the treatment of appendicitis was adopted at the Burbank Hospital in Fitchburg, Massachusetts. This report is an inventory of the subsequent results of this work on one of the two surgical services.

Fitchburg is an industrial city of approximately 40,000 people, surrounded by a considerable rural population. The hospital has 256 beds, of which 86 are ward beds. The ward surgery is managed by two services, each having a chief and two surgeons. The reorganization of the staff and all the work on appendicitis has been done under the direction of two Boston surgeons, and we have frequently had their assistance by telephone, by consultation and at operation. One surgical service is on duty in alternate periods of three months, and all members of the staff, besides carrying on this surgical work, are in general practice.

The principles we have adopted in managing appendicitis fall into three groups,—preoperative, operative and postoperative,—as follows:

**Preoperative Treatment.** The relief of dehydration and shock and the decompression of distention are done before operation whenever indicated. Many patients have been admitted to the hospital in a state of shock and dehydration. The administration of intravenous solutions by the constant drip method is begun immediately and continued until the patient's condition has improved to the point where operation is thought advisable. This treatment is continued through out operation and into the postoperative period. In cases with symptoms of peritonitis with distention, the use of a Levine tube with constant Wangenstein suction is immediately begun. The tube is left in for the operation and as long after it as is considered necessary. It is remarkable how rapidly the condition of these patients improves in a few hours with this management.

**Operative Treatment.** There are two anesthesiologists on the ward surgical service, both of whom have had postgraduate study in anesthesia and are devoting most of their time to anesthesia. We believe that their excellent an-

esthesias have contributed greatly to our good results. We have used spinal anesthesia as often as was possible, otherwise nitrous oxide, oxygen and ether.

A right rectus muscle retracting incision is used in almost every case. In 1 case a McBurney incision was used for the drainage of a palpable abscess. An attempt is made to remove all appendices under direct vision through adequate incisions. The general peritoneal cavity is carefully walled off before any attempt is made to touch the appendix, and suction is used whenever pus is present. Gentleness is constantly stressed. Whenever drains are necessary they are placed to the right of the cecum if possible, and are not removed before the seventh postoperative day. At the completion of the operation when possible, the omentum is pulled down over the operative site. Appendectomy is done as soon as the diagnosis of acute appendicitis has been made or as soon thereafter as the patient's condition warrants. The base of the appendix is tied with two ties, without crushing. The stump is cauterized with carbolic acid, followed by alcohol, but is not inverted.

**Postoperative Treatment.** Clean cases are allowed liquids if there is no nausea or vomiting, in the others, fluids are maintained by intravenous solutions, following the plan of Coller, Dick and Maddock.<sup>1</sup> Cases with drainage are put in Fowler's position and given nothing by mouth or rectum, adequate fluids, and enough morphine to keep them comfortable and quiet. Cases with general peritonitis are put on Wangenstein drainage.

The cases of appendicitis have been divided into three groups: acute appendicitis, where the symptoms and signs were acute, regardless of the pathological findings, recurrent or chronic appendicitis, where there was a history of repeated attacks of pain and where the appendix was reported by the pathologist as showing "healed appendicitis" (routine appendectomies done at the time of other operations were not included), and acute appendicitis with perforation and abscess formation, spreading peritonitis or generalized peritonitis.

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The total number of cases treated was 172. There were 3 deaths, a mortality rate of 1.7 per cent. The mortality was confined to the third group mentioned.

There were 101 cases of acute appendicitis. Appendectomy was done in all cases except 1. This case occurred in a man of seventy-three, with extreme debility, chronic myocarditis and chronic nephritis. There were definite signs and symptoms of acute appendicitis. These disappeared under treatment and the patient recovered, dying three months later of cardiorenal disease. Two cases were complicated by early pregnancy, both patients recovered following appendectomy and went to full-term delivery. There was 1 case in which appendectomy was deferred because of a previous splenectomy for purpura hemorrhagica. When the symptoms increased it was done, with considerable bleeding at operation but with a normal convalescence.

Recurrent or chronic appendicitis occurred in 38 cases. There was no operative mortality.

There were 33 cases of appendicitis with perforation, in 3 of which the patients died, a mortality of 9 per cent. As 1 was not operated on, the operative mortality was 6 per cent. In neither of the operative cases was death due to generalized peritonitis alone. One of these patients, a boy of five, died from acute edema of the lungs within twenty-four hours after operation. Only drainage of the appendiceal abscess had been done. This patient was given nitrous oxide, oxygen and ether anesthesia. Permission for autopsy was not obtained, so that the cause of the edema is unknown. The other patient died five days after operation from a complicating pneumonia, while no autopsy was performed, there was no abdominal distention, and the patient did not present the picture of terminal generalized peritonitis.

In 39 per cent of the perforating appendicitis cases the patients had taken cathartics. Eight had symptoms for twenty-four hours or less, the shortest time being eight hours. In 15 cases two days or less had elapsed between onset and admission, in 2 cases three days, in 3 four days, in 1 each six, seven and twelve days, and in 2 fourteen days.

In the 33 perforating cases there were 41 operations. In 1 case operation was not done because of poor general condition and peritonitis, a ruptured appendix and peritonitis were shown at autopsy. Drainage of an appendiceal abscess only was done in 4 cases, with 1 death. Appendectomy was done three or more months following drainage of an abscess in 3 cases. In 1 case an intussusception was found and reduced, but appen-

dectomy was not done, later three recurrent appendiceal abscesses were opened before appendectomy could be performed, with final recovery. There was 1 case of pregnancy, with recovery and normal delivery at term following appendectomy and drainage.

Table 1 shows the types of appendicitis and of operation, with mortality statistics. Table 2 shows

TABLE 1 *Types of Appendicitis and of Operation*

TYPE OF APPENDICITIS	NO OF CASES	DEATHS NO	PER CENT
Acute	101	0	0
Chronic	38	0	0
Perforated	33	3	9
Totals	172	3	1.7
TYPE OF OPERATION			
Appendectomy	139	0	0
Appendectomy and drainage	26	1	4
Drainage of abscess only	4	1	25
None	2	1	50
Appendectomy after drainage of abscess	3	0	0
Exploratory laparotomy after drainage of abscess (appendix not found)	1	0	0

the postoperative complications in the different groups.

The early diagnosis and hospitalization of most of the 172 cases in this series is, we believe, a great credit to the physicians of our city and has been an important factor in the low mortality rate of 1.7

TABLE 2 *Postoperative Complications*

TYPE OF APPENDICITIS	NO OF CASES	INCIDENCE %	NO OF DEATHS
ACUTE APPENDICITIS			
Total complications	12	11	0
Wound sepsis	4	4	0
Hematoma wound	2	2	0
Postoperative hemorrhage of wound (re-operation)	1	1	0
Phlebitis of right leg	2	2	0
Massive collapse of lung	1	1	0
Bronchopneumonia	1	1	0
Enteritis	1	1	0
CHRONIC APPENDICITIS			
Total complications	4	11	0
Bronchopneumonia	1	3	0
Hematoma of wound	1	3	0
Stitch abscess	1	3	0
Hemorrhagic diathesis (transfusion)	1	3	0
ACUTE APPENDICITIS WITH PERFORATION			
Total complications	12	36	3
Pelvic abscess	5	15	0
Septic wound followed by hernia	3	9	0
Lobar pneumonia	1	3	1
Acute edema of lungs	1	3	1
No operation	1	3	1

per cent. In the delayed cases the physician often had not been called until late. There were very few cases where delay in hospitalization had occurred because of difficulty in diagnosis. The practice of sending patients to the hospital for observation in

all cases in which the presence of appendicitis is suspected is a good one, and should be observed more frequently. A campaign to acquaint the people of Fitchburg with the symptoms of appendicitis, and to impress on them the need for the immediate investigation of abdominal pain the

danger from the use of cathartics and, finally, the importance of time in the successful treatment of acute appendicitis, is urgently needed.

#### REFERENCE

1 Collier F. A., Dick V. S., and Macklock Walter O. M. Intolerance of normal water exchange with intravenous fluids. *J. I. M. A.* 107: 1522-1527, 1936.



## REPORT ON MEDICAL PROGRESS

### COMMUNICABLE DISEASES CARDIOVASCULAR DISEASE IN DIPHTHERIA\*

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THE lowering of the mortality of diphtheria through intubation and antitoxin has centered attention on the cardiovascular disorders of this disease. Malignant diphtheria continues to claim many lives in the early stage, owing to the fact that antitoxin is not given in the first hours. However, even in the recent epidemic years in Europe the malignant type constituted only about 10 per cent of all cases.<sup>1</sup> This type usually involves the fauces and posterior nasal vault with a comparatively low incidence of laryngeal invasion.<sup>2</sup> Nevertheless, the clinician may be confronted by a condition that was for several days only a moderate diphtheria but that, through parental neglect, has assumed an advanced stage by the time of the physician's first visit. It is also possible for a slowly developing type suddenly to assume all the characteristics of a malignant infection. Consequently from a clinical point of view, the term "malignant" may apply to any grave toxemia during the membranous stage.

#### EARLY CIRCULATORY FAILURE AND ITS TREATMENT

It is now generally conceded that early cardiovascular embarrassment is the result of toxemia, and as such differs from that seen in other acute infectious processes only in its possible malignancy and association with respiratory obstruction by the formation of membrane or by edema. It is well recognized that such obstruction is often above the glottis and can be effectively relieved by suction of this area. Too often restlessness, cough and cyanosis are ascribed to cardiac decompensation when actually a piece of freed membrane

lodged in the glottis is responsible. Consequently, lowering the cough reflex with opiates is to be strictly avoided in the membranous stage.<sup>3</sup> This general intoxication, then, is the same as that seen in other septic conditions unless respiratory obstruction creates a strain on the heart through violent respiratory efforts in the presence of anoxemia. There are fever and tachycardia. Difficulty or pain on swallowing often results in dehydration. The carbohydrate metabolism is disturbed in proportion to the toxemia. At first the glycogen is rapidly used up, giving rise to a decreased sugar content of the blood. If the toxemia is prolonged, this condition may change abruptly to an increased blood sugar due in part to suppression of insulin but also to inability of the tissues to assimilate dextrose.<sup>4</sup> The blood pressure continues near normal<sup>5</sup>, the heart sounds are distinct and usually continue to be regular unless death is imminent. Finally, there is anemia of the medullary centers.

Leete<sup>6</sup> has reviewed 4700 cases of faucial diphtheria which occurred during the recent epidemic in Hull, England. Among these there were 461 fatalities. In those patients who died early in the disease the general toxemia overshadowed any cardiac disturbance as a cause of death, an observation in accord with that of Gordon<sup>7</sup> at Detroit and my own in Boston.

The treatment here is not directed at the heart alone, because this organ is simply being poisoned along with other vital centers. Consequently the best supportive measures consist of the vigorous administration of antitoxin, together with intravenous injections of 10 per cent dextrose—100 to 500 cc. according to the age of the patient. The use of insulin in conjunction with dextrose has been shown to be ineffective by the controlled clinical observations of Begg.<sup>8</sup> In cases of very

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severe toxemia some physicians have given 30 cc of 50 per cent dextrose in the first dose, using 10 unit of insulin intramuscularly with each gram of dextrose. At the Haynes Memorial Hospital we prefer the 10 per cent solution because dehydration is always present. A word of warning should be given in regard to the antitoxin. Of course, these severe cases need the maximum scale of dosage, and it is always desirable to introduce part of the antitoxin intravenously, but if circulatory collapse is already in progress great care must be taken not to cause a further drop in the blood pressure. Adrenalin must always be at hand. To offset circulatory collapse one may give the antitoxin either intravenously, diluted with 200 cc. of normal saline, or intramuscularly in the lateral aspect of the thigh, diluted with 100 cc of normal saline. It should be administered very gradually, as is done in those individuals showing serum sensitivity to the preliminary skin test.

As for drugs, there is nothing to be said in their favor. Opiates, as has already been mentioned, are to be avoided in the membranous stage. The same applies to all sedatives. The natural state in this stage is one of apathy unless there is a mixed infection with a streptococcus. If, therefore, restlessness occurs it is likely to be the result of obstruction to breathing in one form or another. Suction, intubation or tracheotomy may be necessary, but the indications for these will be masked by opiates. Efforts directed at stimulating the circulation to the neglect of respiratory obstruction are poor medical practice. On the other hand, if no obstruction is present the profound toxemia causes death. Digitalis, as well as all the drugs of the digitalis group, is ineffective, if not actually harmful, owing to the possibility of the occurrence of beginning myocardial necrosis and inflammation. Furthermore, the heart poisoned by diphtheria is unusually susceptible to the action of digitalis,<sup>8</sup> and block may be induced. Camphor in oil, caffeine and Coramine have been found to be futile. The latest experimental and clinical studies<sup>9-16</sup> on the use of vitamins in diphtheria offer no encouragement.

#### LATE CARDIOVASCULAR DISORDERS

A certain amount of confusion has crept into the literature in regard to the use of the term "late" as applied to cardiovascular disorders. In the first place, arbitrary periods in terms of the day of the disease are used to differentiate early and late. Secondly, the term "circulatory failure" has been used to embrace disorders which may or may not lead to true circulatory failure. Finally,

too much effort has been expended in attempting to make a constant syndrome out of late circulatory failure when, as a matter of fact, it can be brought about through divergent pathologic processes that may operate either independently or in conjunction with each other.

**Cardiac Involvement** In the malignant type of diphtheria, which overwhelms the patient from the beginning, evidence of myocarditis may appear as early as the third day. On the other hand, in the clinical type that has a more gradual or smoldering onset the signs may not appear until the fourth or fifth week. Furthermore, the promptness with which antitoxin is administered in either of these types may prevent, delay or modify the manifestations of cardiovascular damage.

Some confusion exists in the use of the term "malignant" because it has come to be applied in a bacteriological rather than a clinical sense. Thus, an epidemic in which the gravis strain predominates is described as an epidemic of malignant diphtheria even though only about 10 per cent of the total cases exhibit the fulminating type. Here we have mild cases designated as malignant because of the epidemiologic characteristics. The term "malignant" is used in the present paper in its clinical sense according to the well-known classifications of Marfan and Destéfano,<sup>17</sup> and not according to the presence of the gravis strain.

The term "late" as applied to cardiovascular disorders is employed here to denote that convalescence from the membranous stage is under way. The local lesion is undergoing repair or is entirely repaired, yet the bound toxin or its by-products in the tissues continue to influence the cardiovascular system. This can occur where a spontaneous recovery takes place without the administration of antitoxin. Myocarditis is the outstanding pathologic feature, and is present in most cases when circulatory failure occurs. The earlier the signs of myocarditis, the graver the prognosis. However, myocardial insufficiency is frequently only a contributory cause of death, in that paralysis of the vasomotor system is oftener the direct cause of the complete circulatory failure.

✓The earliest signs of myocarditis are found in the electrocardiogram.\* In fact, it may show a high degree of heart block before this is suggested by clinical observations, and such observations clearly indicate impairment of the cardiac

\*Observations on the oculocardiac reflex by Borgiotti<sup>18</sup> showed that electrocardiographic changes were induced which were not observed in the electrocardiogram taken before the test, suggesting that mechanical compression of the eyes brings out latent cardiac pathologic defects. Frontali<sup>19</sup> is of the opinion that this phenomenon is due to the effect of the diphtheria toxin on the nervous system and is therefore of extracardiac origin.

function<sup>20-22</sup> It is in these cases that cardiac failure may come on with great rapidity and lead to the death of the patient Natin and da Rin<sup>17</sup> in 1934 published a very extensive series of electrocardiographic records on 144 cases, embracing all the characteristic alterations found in diphtheria, with numerous modifications, and now serving as a standard reference work. Indeed, it is only by the electrocardiograph that one can properly determine the extent of the cardiac damage, knowledge so essential to the prognosis as well as to the duration of strict aftercare.

*Symptoms and Signs* With this in mind let us review as they appear the clinical symptoms, the electrocardiographic findings, the physiological and pathological situations which may confront us and the means which we have of dealing with them The fact has already been stressed that the electrocardiograph picks up the first signs of damage to the myocardium, but of course the instrument is applied only from time to time. The clinician can usually determine the presence of cardiac injury without it, but he cannot thus determine the exact nature of the injury to the conduction system This applies especially to auriculoventricular dissociation with ventricular tachycardia,<sup>23</sup> which frequently leads to a fatal termination The first sound becomes soft, and is frequently replaced by a systolic murmur with a maximum intensity to the left of the sternum, or the first or second sound may be split Cardiac dilatation can at times be quite obvious Andersen<sup>21</sup> determined the existence of myocarditis clinically in 49 of 194 cases of severe diphtheria, in 60 of which the electrocardiograms showed evidence of the condition Any irregularity of rhythm may take place, but the commonest change noted is a protodiastolic gallop In certain cases this gallop varies greatly in its intensity

In the convalescent stage, while the patient is often in a comfortable and cheerful state, he may suddenly develop epigastric pain vomiting, pallor and a characteristic frightened look The heart rate may be accelerated at first, and then become gradually slower and irregular, or it may continue to be rapid The pulse is soft, and sweating may be pronounced Sometimes the patient goes through several of these crises, in which the blood pressure may vary above and below normal In such cases periods of ventricular fibrillation have preceded death<sup>17</sup> In fatal block the heart rate is likely to drop below 30 and with this there is sometimes precordial pain

Electrocardiograms may show every variety of grave disturbance to the conduction system, both auriculoventricular and intraventricular (bundle

branch) block Like gallop rhythm, the block may come and go, but its presence implies much greater danger than does the gallop Place,<sup>6</sup> Alstead<sup>22</sup> and Burkhardt<sup>22</sup> are of the opinion that cases in which the electrocardiogram shows evidence of myocarditis without block invariably recover under proper treatment Nathanson<sup>4</sup> on the other hand, reported 2 sudden deaths in convalescents showing inverted T waves Von Koss,<sup>25</sup> from his large recent experience in Budapest, states that damage to the musculature as shown in pronounced changes in the T wave with only slight or questionable involvement of the conduction system as shown by lowering of the QRS complex may signify impending danger, further, that an inverted T wave in all three leads, or at least in Leads 1 and 2, means without doubt a severe myocardial lesion with a probable fatal outcome Alterations in the T wave are usually seen first in Lead 3 then in Lead 2 and finally in Lead 1 T wave alterations—biphasic, isoelectric and inverted—are at times found in other infections, such as tonsillitis, scarlet fever, typhoid fever and pneumonia, but they are probably of graver significance in diphtheria In diphtheria a combination of damage to the specialized conduction system and of injury to the myocardium in general is common Conduction changes are more frequently observed in early childhood, while alterations in the T waves are more prevalent in older patients<sup>22</sup> Bock<sup>24</sup> lays emphasis on a lengthened QT interval

The advent of marked block usually precedes signs and symptoms of circulatory failure Under these circumstances death may occur within a few hours, or be delayed for several days after increasing weakness If myocardial insufficiency predominates there are cardiac dilatation cyanosis with mottling, sometimes cough and rales, extreme restlessness, epigastric pain, vomiting and enlargement of the liver Myocardial insufficiency may occur without block, in which case there is increasing tachycardia Heart block may appear and disappear several times during the day This form of cardiac failure usually occurs in the first or second week of the disease

Lesser disturbances of rhythm such as extra systoles may be occasioned by irritation of the myocardium but also by the action of the toxin on the parasympathetic nerves This also applies in part to mild variations in the rate, in the form of relative tachycardia, bradycardia and cardiac irritability<sup>7</sup> A lowering of the tone of the sympathetic control is sometimes accompanied by marked lowering of the white-cell count, with a relative lymphocytosis In fact these findings

have served as a warning of impending vasomotor collapse<sup>2</sup>

*Peripheral Circulatory Failure* While myocarditis of some degree is almost invariably found at autopsy in late circulatory failure, it is, as we have already remarked, oftener only a contributory cause of death, the commonest cause being vasomotor paralysis. This paralysis is not of central origin but is in the myoneural junction or motor end plates of the parasympathetic nerves of the splanchnic vessels, being a manifestation of the polyneuritis that constitutes postdiphtheritic paralysis. Thus, it coincides with the onset of other paralyses such as the palatal and oculomotor. Furthermore, it is not to be confused with respiratory paralysis involving the phrenic and intercostal nerves, in which the respirator may be the means of saving the patient's life.

Vasomotor paralysis is in itself the commonest vascular syndrome complicating diphtheria, and this extracardiac condition, even in the presence of advanced myocardial damage, tends to overshadow disorders arising within the heart. The syndrome consists of marked pallor, in which the patient takes on a gray color or that resembling alabaster, along with a peculiar frightened look in children. The skin becomes cold. There is epigastric pain with vomiting. Without block the heart tends to become rapid as the blood settles in the relaxed and engorged splanchnic vessels. The volume of blood in the heart is diminished, and the blood pressure falls. With well-marked heart block, the chambers have time to fill and the pulse can be obtained, otherwise it is likely to be lost. In a few hours the patient may be dead, or this condition may continue for several days and then lead to a sudden fatal termination or to recovery.

*Intracardiac Thrombosis* One type of myocarditis which occasionally occurs in the very toxic form of diphtheria is that associated with the formation of a thrombus, a condition resulting from extensive inflammation or hemorrhage within the myocardium and the overlying endocardium in conjunction with dilatation. Of course, the pathologic state of severe diphtheria, like that of severe scarlet fever, includes a hemorrhagic tendency, and it is not surprising that this should appear in the heart itself. I have seen a large, pendulous thrombus originating in the left auricle, reaching well into the mitral orifice and before death giving rise to an indescribable clatter of heart sounds. Chirri<sup>28</sup> describes one of these cases which at autopsy showed marked fatty degeneration and a thromboendocarditis, from which diphtheria bacilli

were recovered in pure culture. In a later communication<sup>29</sup> he reports the autopsy of a ten-year-old girl who with extensive membrane died suddenly on the fifth day from "heart collapse," without any previous signs of cardiac disorder having been noticed. The heart showed marked fatty degeneration, with many hemorrhages under the epicardium, in the myocardium and under the endocardium. These were particularly marked in the right auricle in the region of the sinus and the atrioventricular node. There was marked cardiac dilatation, especially on the right, and the mitral valve showed a fibrinous exudate from which was obtained a pure culture of diphtheria bacilli. Harding<sup>30</sup> reports no less than eight attached blood clots found within heart chambers at autopsy. Such thrombi may be the source of emboli that are carried to various organs, giving rise to repeated infarctions in the brain or lungs, with sudden hemiplegia and pulmonary signs.<sup>2</sup> According to Rolleston,<sup>31</sup> hemiplegia, in contrast to other palsies arising from diphtheria, has its origin primarily in damage to the blood supply by embolism, thrombosis or hemorrhagic encephalitis, of which embolism is the commonest. The difficulties in diagnosing cerebral emboli are discussed by Zischinsky<sup>32</sup> in a review of 14 cases from his Vienna clinic.

*Endocarditis* Vegetative endocarditis of the mitral valve from which the diphtheria bacillus was recovered in pure culture has been reported<sup>33-35</sup>. It is true that in 1 of these cases<sup>33</sup> a previous rheumatic endocarditis existed prior to the onset of diphtheria. But it is significant that the diphtheria bacillus set up a local process in this already damaged valve, causing death. A true vegetative endocarditis in the course of diphtheria is an extremely rare phenomenon, therefore, the heart murmurs usually heard are not due to valvular endocarditis.

*Postdiphtheritic Neurocirculatory Asthenia* A mild but disturbing cardiovascular disorder may occur in the late convalescence of some cases of diphtheria. I refer to a curious irritability of the pacemaker which often results in an evening tachycardia persisting for three to eight weeks. This can happen when vascular collapse has not taken place and when the myocardium has escaped injury. It may also take the form of a persistent relative tachycardia or bradycardia or an "effort syndrome," being similar to the condition sometimes following other infections such as typhoid fever and influenza. It may have its origin within or outside of the heart, that is, in the sinus node or in the parasympathetic vagus nerves.

## PATHOLOGIC CHANGES

The pathologic changes found in early circulatory failure in diphtheria are due to an overwhelming toxemia, and sometimes include dilatation of the heart. Massboff,<sup>36</sup> in a postmortem study of 20 hearts, found that dilatation of the auricles was greater than that of the ventricles, and that the bicuspid valve was most frequently dilated, the right side of the heart being more involved than the left, as shown by microscopic sections. However, such changes are by no means constant, and one may often search in vain at autopsy for evidence of injury in the heart or anywhere in the nervous system as even a contributory cause of death.<sup>37</sup> In a more prolonged toxemia the myocardium may begin to show parenchymatous hyaline degeneration or necrosis. The longer the myocarditis lasts before death occurs, the more pronounced and extensive this change becomes.<sup>38</sup> The toxin seems to show no partiality for either the conduction system or the contractile tissues. Friedemann<sup>37</sup> is of the opinion that the toxin of diphtheria injures the walls of the coronary vessels, and that in time this brings about disturbances in the conduction system, thus explaining the latent period. The evidence of true myocarditis consists of necrosis and the inflammatory process of repair. Complete regeneration or fibrosis may follow. Sometimes the inflammatory infiltration as part of the process of repair appears to choke the nutrition of the healthier muscle fibers.<sup>39</sup> Occasionally the heart appears normal until careful search shows a small inflammatory area about the bundle. Deaths in these cases were formerly attributed to vagus degeneration. At other times, the extent of myocardial damage found at autopsy is astonishing. Occasionally such large patches of fatty degeneration are observed that it makes one wonder how the heart could have continued beating so long.

## DURATION OF CARDIAC DAMAGE

Findings at routine postmortem examinations strongly suggest that some individuals long since recovered from diphtheria may carry permanent scars through life in the form of areas of fibrosis in the myocardium.<sup>39</sup> However, this can be taken only as presumptive evidence of permanent damage from diphtheria. The temptation of many observers has been to correlate these late findings with the large areas of fatty degeneration mentioned above. I once held the view that permanent cardiac damage was to be expected. Recent evidence on the duration of myocardial damage after diphtheria has caused me to alter my opinion.

In 1905, F. W. White<sup>40</sup> reported on 78 cases examined by him six to twelve months after they had exhibited heart complications during diphtheria. He pointed out that a return to normal in some severe cases required weeks or even months. Many subsequent observers have determined that recovery promises complete regeneration of the heart muscle so that eventually the electrocardiogram becomes entirely normal, even though the heart may continue to show the effects of injury for months. Mautner<sup>41</sup> reports a typical example, in which block persisted for eighteen months. Von Kuss<sup>42</sup> reports a case in which heart damage persisted for five years after diphtheria, and another in which bundle branch block with myocardial insufficiency persisted for ten years.

Andersen<sup>43</sup> examined 24 patients eight years after recovery from diphtheria, none of whom had had any infection in the intervening period that would suggest myocardial involvement. Among 15 with definite electrocardiographic changes during diphtheria, 7 continued to show these changes. Among 12 who showed clinical signs of myocarditis during the attack, 4 continued to show signs of myocardial insufficiency. In all, 16 patients showed abnormal electrocardiograms. Andersen supports his observations by referring to Schwenken<sup>44</sup> who in 1922 drew the conclusion that diphtheria must be considered an important cause of heart failure in later life. The criteria on which he bases this statement cannot be considered as first rate evidence, and he admits that in some of the cases studied only doubtful signs of myocarditis existed at the time of their stay in the hospital with diphtheria.

Alstead<sup>45</sup> studied 150 patients who were known to have had severe diphtheria. In 90 of these he found a negative or isoelectric T wave in Lead 3, whereas this was found in only 30 of his 100 controls. He acknowledged that this finding could not be accepted as evidence of myocardial disease and pointed out that regardless of whatever its significance might be there was certainly no consistent clinical abnormality.

Jones and P. D. White<sup>46</sup> in 1927 studied 100 patients who had suffered from severe diphtheria five to ten years previously at the Boston City Hospital. 12 of whom were originally diagnosed as having had myocarditis. Clinical, radiographic and electrocardiographic examinations failed to reveal any appreciable chronic effect of the disease on the heart. Ninety-one of these patients were re-examined after another ten years by Thompson, Golden and P. D. White,<sup>46</sup> and 9 more were added from the original period to make up an even 100. In none of these was there any



positive proof of abnormalities resulting from the diphtheria, nor had evidence of any cardiac disturbance resulting from it made an appearance within the interval of fifteen to twenty years. These cases are to be studied again in 1947.

The term "myocarditis" is often used loosely to denote circulatory failure. A relatively mild myocarditis associated with vasomotor collapse would not be expected to give rise to as lasting myocardial damage as a more severe myocarditis in which vasomotor collapse was averted. There must always be an element of doubt regarding the diphtheritic origin of heart disease developing in later years where no myocarditis existed during or immediately after the diphtheria. Therefore, with due consideration of our knowledge of the pathology and the process of repair, particular interest centers in the subsequent history of those cases exhibiting indisputable signs of severe myocardial injury as a result of diphtheria.

In 70 cases of severe diphtheritic myocarditis treated at the *Plauen Stadtkrankenhaus*, Behr<sup>46</sup> continued the electrocardiographic examinations in the survivors for a period of two years. He found that damage to the musculature of the auricle, as suggested by abnormalities in the P wave, was restored more quickly than was damage to the ventricle. Patients with a continued complete block and slow ventricular rhythm invariably died, while those in which the complete dissociation lasted only a minute or two often recovered. During the shift from partial to complete block with a long ventricular pause the Morgagni-Adams-Stokes syndrome developed. One block continued in evidence for months but cleared up entirely in two years. Bundle-branch block, with its sudden and so often fatal outcome, was usually slow in clearing up, but even here the survivors eventually showed a complete return to normal. Changes in the T wave during the acute disease usually appeared first in Lead 3 and then in Leads 2 and 1. But in this event, if the patient survived the early period, there was a tendency for the T waves to revert to normal in the course of days or weeks. At the follow-up electrocardiographic examinations one and two years later there was nothing to suggest organic or functional heart disease. It is to be hoped that these cases, so carefully followed from the start, will be followed up in the same manner that is being carried out by Dr. Paul D. White and his associates.

It is always difficult to prove that a myocardial failure developing in later life is related to a severe diphtheria of childhood.<sup>45, 47</sup> Circumstantial evidence is supplied by Butler and Levine<sup>48</sup>

in a group of 20 patients having proved heart block without the usual causes, such as arteriosclerosis, syphilis, coronary disease, digitalis, fever and rheumatic infection. However, congenital block could not be ruled out in this small group. Fifty per cent of the patients had a history of diphtheria in childhood, as compared to 6 per cent in 600 consecutive control surgical cases. The average age of the patients who had had diphtheria was eleven years lower, and their average systolic blood pressure was 40 mm. lower, than in those who had not. Reid<sup>49</sup> cites a girl of ten who showed a permanent bradycardia, presumably dating back to a severe attack of diphtheria five years previously. She was leading a normal life. Faulkner<sup>50</sup> reports 2 cases with permanent abnormalities dating back to diphtheria, one patient was a machinist leading a normal life with a high take-off of T<sub>2</sub> and a prolonged PR interval, and the other a woman leading an active life who had passed through an uneventful pregnancy with a complete heart block.

With the evidence at hand one is forced to conclude that if the heart has shown no signs of impairment within six weeks of the attack of diphtheria, there is as yet no definite proof that it will be more prone to heart disease in later life. Furthermore, when injury to the muscular or conduction system fails to cause death at the time of the myocarditis, the tendency is toward complete recovery. The muscular system generally returns to normal more promptly than does the conduction system, bundle-branch block being the slowest to recover. True myocarditis of diphtheria is an inflammatory response to degeneration, and as such is a process which tends either to kill or to permit a return to normal. Rare cases of permanent block are on record, but most of these are not attended with myocardial insufficiency. Whether a persistent, purely functional defect leads to impairment later in life is as yet unknown. Well-controlled investigations are under way, and one awaits with great interest the reports from carefully followed cases as the patients pass the age of fifty.

#### INCIDENCE OF SEVERE CIRCULATORY DISTURBANCE

The incidence of myocarditis in diphtheria can be seen in Table 1, comprising 15,490 cases compiled from hospital records in three American cities. The term "myocarditis" as used here is based largely on the clinical diagnosis, with an indefinite amount of support from electrocardiograms and autopsies, which after all constitute the final criteria for this diagnosis. Hoyne and

Welford<sup>11</sup> found that the mortality rate in cases showing myocarditis was 75 per cent in patients under five years of age, 54 per cent in those from six to ten, 50 per cent in those from eleven to fifteen and 43 per cent in those over fifteen. As regards the relation of the type of diphtheria to the death rate, it was found that in the simple

myocarditis appear, the more serious is the prognosis.

The routine use of the electrocardiograph on diphtheria wards is sure to give a much greater recognition of myocarditis than has hitherto been obtained by routine clinical examinations and electrocardiograms of severe cases only. Under

TABLE 1 Incidence of Clinical Myocarditis and Mortality in Diphtheria in Three American Hospitals

AUTHOR	HOSPITAL AND LOCALITY	N. OF CASES OF DIPHThERIA	No. OF DEATHS FROM DIPHThERIA	MORTALITY %	No. OF DEATHS WITH MYOCARDITIS AS A CONTRIBUTORY CAUSE	MYOCARDITIS MORTALITY IN RELATION TO TOTAL DEATHS %
Horne <sup>12</sup>	Metropolitan, Chicago	4671	518	11.6	302	56.2
Gordon <sup>13</sup>	Herman Kiefer, Detroit	4751	599	12.6	373	62.6
Wesselhoeft	Haynes Memorial, Boston	6068	602	9.9	356	59.1
Totals		15490	1719		1039	
Averages				11.3		59.4

1. These three series, myocarditis as a cause of death is very much the same, as seen by the figures in the last column. In the recent European epidemics of malignant diphtheria myocarditis and acute toxemia became more frequent cause of death, while laryngeal diphtheria diminished in this respect.

tonsillar form the mortality rate was only 11 per cent, as compared with 54 per cent when the membrane had spread to the uvula and pharynx and 70 per cent when it had spread also to the nose.

Thoenes<sup>14</sup> analyzed 1124 cases of diphtheria at Cologne during 1929-1930. One hundred and eighty-six patients (16.5 per cent) showed severe circulatory disturbance, and 54 of these (29 per cent) died. The original infection in the fatal cases was severe in 47, moderately severe in 4 and apparently mild in 3. Death occurred in 11 cases between the second and seventh days, in 33 cases between the eighth and fourteenth days and in 9 cases between the fifteenth and twenty-third days. One patient died on the forty-second day. Thoenes's classification of early and late failure differs from mine in that the late form includes only those arising at the time of postdiphtheritic paralysis, a method of grouping used in various European clinics.

Behr<sup>15</sup> in Plauen, studied 230 patients with malignant diphtheria, of whom 84 (36 per cent) died. His electrocardiographic findings and follow up results have been mentioned above. Among 70 children, myocardial changes appeared in the first week in 28 cases, and of these patients 24 died of heart failure, 2 died of respiratory paralysis and 2 survived. In the course of the second week 35 patients developed myocarditis, 2 of whom died of heart failure, 1 died of respiratory paralysis and 32 lived. During the third week 7 patients developed myocarditis, and only 1 of these died. Thus we see that the earlier the signs of

sen<sup>11</sup> selected 194 moderate and severe cases for electrocardiographic study. He found that only 24 per cent of those with moderate diphtheria and 11 per cent of those with the severe type failed to show evidence of myocarditis. This study was made in 1933 in Copenhagen, where malignant diphtheria was prevalent and where the incidence of myocarditis would consequently be high.

In an extensive study of 144 cases of diphtheria in Buenos Aires, Natin and da Rin<sup>17</sup> found electrocardiographic alterations in 62 cases, as shown in Table 2. On the other hand, in New York City recent serial electrocardiograms of 140 patients

TABLE 2. Electrocardiographic Alterations in Relation to Type of Diphtheria (Natin and da Rin<sup>17</sup>)

TYPE OF DIPHThERIA	ELECTROCARDIOGRAPHIC ALTERATIONS %
Mild tonsillar (without edema)	7.6
Severe tonsillar (with edema)	13.0
Submalignant unilateral, facial	25.0
Submalignant bilateral, facial	42.0
Malignant, slow	79.4
Malignant, rapid and hemorrhagic	100.0

showing toxic diphtheria manifested alterations in only 28%. It is difficult to attribute these wide variations in electrocardiographic findings entirely to the relative prevalence of malignant diphtheria in these different parts of the world. Obviously this clinical type gives rise to a greater incidence of myocarditis, but it is equally obvious that the electrocardiographic interpretations made by Burkhardt and his associates in New York City are more

conservative than those of Andersen at Copenhagen. A greater uniformity in these interpretations is therefore desirable in establishing the incidence of myocardial damage, which plays such an important part in the severe circulatory disturbances of diphtheria.

The number of possible combinations of functional disease makes it impossible to lay the blame for late circulatory failure on any one factor, or to expect any uniformity in the clinical picture. Furthermore, these disturbances frequently arise so late—and as part of the postdiphtheritic polyneuritis—that their clinical counterpart is inapplicable to those animal experiments dealing at most with a merging of the toxic stage with myocardial injury. Indeed, I am reminded of the statement of Friedberger<sup>63</sup> that natural diphtheria in man is as different from the toxin-produced diphtheria in the guinea pig as a man is from a guinea pig. This applies equally well to experimental circulatory failure in animals and the late circulatory failure observed in man. Such a clinical point of view in no way belittles the work of Enriquez,<sup>64</sup> Romberg,<sup>65</sup> Porter,<sup>66</sup> Yabe<sup>67</sup> and Edmunds<sup>68-70</sup> and others, any more than it belittles the mass of invaluable data afforded by animal experimentation in the entire field of diphtheria. It merely draws attention to the limitations of their clinical applicability.

#### TREATMENT OF LATE CIRCULATORY DISORDERS

In the treatment of late circulatory failure in diphtheria there are many possibilities to be considered, and therefore no hard and fast rules of management can be laid down. Actually, in every case it must be decided whether failure exists or is threatening. The mere presence of dysfunction as manifested by gallop rhythm or mild conduction disturbances demands no more than complete rest in bed. On the other hand, any moderate amount of diphtheritic membrane in the initial stage is a potential source of late cardiovascular disorder, and any severe formation of membrane requires prolonged bedrest, preferably with hospital facilities. Early and adequate treatment in the acute stage will do much to prevent late circulatory failure.

Once the seriousness of the situation is established through signs and symptoms, any one of the combinations of cardiac abnormalities is a possibility, with or without disturbed peripheral circulation, splanchnic congestion and oligemia. As regards the myocardial condition, the question arises as to whether digitalis is indicated. The functional disturbance here can be so similar to that observed in acute digitalis poisoning that

one would hesitate to consider any dosage that would fulfill the term of "digitalization," since further blocking is to be feared. If small doses are to be used, how small must these be in order to avoid danger? The answer of most clinicians is to advise against employing it at all, with which I am in agreement, in spite of evidence that this drug is capable of exerting its beneficial influence on the undamaged areas of the heart. The reason for this stand is that although the drug might be helpful on one day, the situation might be so altered on the next as to contraindicate it without means of counteracting its influence. Such competent clinicians as von Bokay<sup>2</sup> and his successor, von Koss,<sup>60</sup> in Budapest, have given small daily doses with careful electrocardiographic controls in the earliest stage of myocardial dysfunction, but any attendant improvement in the metabolism of the heart muscle which they ascribed to it was probably due to the dextrose administered intravenously in combination with this drug. Digitalis is therefore contraindicated, and this applies to all other drugs of the digitalis group. However, in the later weeks of convalescence, if signs of decompensation appear, digitalis should be tried cautiously. There is no advantage in using the less standardized drugs of the group, such as ouabain and strophanthus. Alcohol, caffeine, camphor, strychnine and Coramine continue to have their advocates, but in my hands they have proved valueless.

I now come to a consideration of the disturbed peripheral circulation due to vasomotor paralysis with relaxed splanchnic vessels and oligemia. This syndrome appears rather abruptly. There is logic in the assumption that adrenalin might be helpful, but the condition is always too far advanced to yield to this drug. Then again, there is logic in the use of Pitressin (beta hypophamine) with low blood pressure. It has a longer and more powerful action than has adrenalin. Gordon<sup>3</sup> has found it of value in subcutaneous doses of 0.25 to 1.00 cc at eight-hour to twelve-hour intervals, being guided by blood-pressure readings. These doses must always be preceded by the giving of fluids or, in the event of vomiting, by intravenous injections. He used 10 per cent dextrose—100 cc for an infant, 500 cc for a child, 1000 cc for an adult each day. Schwentker and Noel<sup>61</sup> see no justification for forcing fluids in this later circulatory collapse, but they do not consider the simultaneous use of Pitressin. My experience at the Haynes Memorial Hospital has not suggested that intravenous dextrose alone is of any appreciable value in late vasomotor paralysis. Furthermore, it is worthy of mention that one may encounter great difficulty in getting the

needle into a collapsed vein, especially in the case of a small child Dieckhoff<sup>14</sup> found that Ventol (Paredinol\*) raised the blood pressure in late vascular collapse both in animal experimentation and at the bedside. There were 4 deaths among his cases attributable to myocarditis, which was established by the electrocardiograph.

During the last twenty five years a number of other measures have been advocated for this condition. Among these, the use of an abdominal binder and the raising of the foot of the bed, as recommended by Harding,<sup>10</sup> seemed particularly hopeful. At the Haynes Memorial Hospital raising the foot of the bed never appeared to accomplish anything. On the contrary, children would exhaust their waning strength in getting into a more comfortable position. The binder still meets with favor. Another simple measure which at times seems at least temporarily helpful is to supply warmth in cases where the color becomes alabaster and the skin cold. This can be done with hot water bottles or a wire-covered electric light bulb. In some cases a pink color actually returns. Friedemann<sup>17</sup> used baths, working the temperature up from 35 to 39°C (97 to 104°F). I have tried vigorous friction many times, but never with success. Of all the many measures employed in various parts of the world to combat circulatory collapse, the only one that has consistently reduced the mortality in hospitals is the vigorous intravenous administration of dextrose in all advanced cases of diphtheria. As with antitoxin the beneficial action of this substance is essentially protective.

How long after recovery from circulatory disorders should a patient be kept in bed? The answer depends on the severity of the disorder and the duration of signs and symptoms, generally speaking, the patient should remain in bed until the electrocardiogram has become normal.<sup>12</sup> Roughly, all patients with severe diphtheria with evidence of myocarditis should be kept in bed for six to eight weeks, and those without electrocardiographic control or clinical signs of myocarditis for four or five weeks. Patients in my service showing a postdiphtheritic neurocirculatory asthenia, in the absence of any evidence of myocardial damage, are generally kept in bed four weeks. After this they are allowed out of bed, with their activities restricted according to the behavior of the heart. Medication is quite unnecessary. Adults should have the condition carefully explained in order to gain their confidence and co-operation.

In conclusion, I believe that late circulatory fail-

ure presents such a complication of possibilities that every effort should be made to determine the predominating factors and to try to correct these with the most direct and simple measures. A prolonged rest in bed of at least six to eight weeks is the proper safeguard during the repair of severe cases. It is needless to say that the proper facilities for the care of cardiovascular disorders in the course of diphtheria exist only in a hospital equipped for the purpose.

The author expresses his indebtedness to Dr. Paul D. White for much valuable criticism of the manuscript and for the clarification of many uncertainties in the field of cardiology which best one who deals with the problems of acute infections.

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\*Paredinol is Smith, Kline and French's trade name for racemic parathyroid-N-dimethyl phenethylamine referred to abroad under the name Ventol (Kao 11-75).

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 26281

### PRESENTATION OF CASE

*First Admission* A twenty-two-year-old single girl student was admitted to the hospital complaining of weakness.

The patient was in fairly good health until two years before admission, when she began to urinate easily and complain of insomnia and weakness which steadily progressed. She had had amenorrhea for five years, and before this time the menses had been irregular and scanty. Approximately six months before admission she was treated for two months with liver extract for anemia, which was thought to have possibly resulted from frequent epistaxes which she had experienced all her life, on occasions she bled as much as 2 ounces or more. About one month after liver therapy was stopped, she noticed a general bronzing or yellowing of the skin, the scleras were not jaundiced. No change in the color of the urine or clay-colored stools appeared. There were no puritus, abdominal symptoms, indigestion, weight loss, dyspnea, palpitation, cough, hemoptysis or night sweats. One week before entry, when seen by a physician, bile was discovered in the urine.

The family and past histories were non-contributory.

Physical examination revealed a fairly well developed and well nourished woman in no apparent distress. The skin was evenly brown, without blotching, or increased pigmentation in the axillae, it was greasy, with an acneiform eruption over the face and chest. There was hypertrichosis of the arms, face and abdomen, with masculine distribution of the pubic hair. The head hair was stiff and dry. The mucous membranes were pale, with no abnormal pigmentation. The scleras were slightly jaundiced. The heart, lungs, abdomen and remainder of the examination were negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 3,400,000 with 70 per cent hemoglobin, a white-cell count of 4000 with 67 per cent poly-

morphonuclears, a normal smear, and a reticulocyte count of 1.9 per cent. The urine and stools were essentially negative, one specimen of urine gave a + test for bile. A blood Hinton test was negative. The icteric index was 35 per cent, the van den Bergh 6.8 mg bilirubin per 100 cc., bi-phasic reaction, the bleeding time 3 minutes, the clotting time 7 minutes. A liver function test showed 90 per cent of the dye retained. A sugar tolerance test showed an elevated flat curve fasting 78 mg per 100 cc. half an hour, 124 mg, an hour, 230 mg, an hour and a half, 200 mg. A blood fragility test was normal.

On the twelfth hospital day an exploratory laparotomy revealed a definitely cirrhotic liver with a large smooth spleen, four times the normal size, and dilated epigastric veins. An omentopexy was performed. The patient was discharged improved on the thirty-first hospital day.

*Second Admission* (seven years later) After discharge, the patient was reasonably well, save for a persistent pigmentation of the skin, frequent epistaxes and decreased resistance to infections. Three years before this admission the epistaxis had been relieved by cauterization of small nasal blood vessels. About four years before admission her ankles began to swell daily. There were no other signs of cardiac embarrassment. No ascites was noticed. Two years before admission the patient was treated for acute gonorrheal vulvovaginitis. She continued to be active, although on rare occasions she was forced to stop work because of extreme fatigue. For three to four months before entry, in the evenings the patient's legs were swollen up to the hips but by morning most of the edema had disappeared. Two months before entry, after a period of extensive mountain climbing and bicycling, she developed chills, fever ranging to 102° and 103°F., malaise, anorexia and night sweats, but no definite pain, cough, vomiting, diarrhea or joint trouble. This infection lasted for two weeks and then gradually subsided, with recovery of strength and spirit, so that three weeks before admission the patient returned to work. Ten days before entry she developed fatigue, and four days later, while enjoying a week-end holiday, she began to feel "dopey," feverish and nauseated. She retired to bed, and suddenly began to experience crampy pains over the abdomen, most marked below the umbilicus and associated with the passage of four to five watery stools. The diarrhea increased to seven or eight times daily, and four days before admission she had a temperature of 101.5°F. A physician found a dull distended abdomen, with right lower-quadrant ten-

derness and, by rectal examination, extreme tenderness of the cervix. During the three days before admission the abdominal pain increased, spread to the epigastric region and extended to the lower costal regions anteriorly, especially on the right. Alternate constipation and diarrhea began to appear.

Physical examination revealed an acutely ill, well-developed, fairly well-nourished woman. There was a generalized dirty-brown pigmentation of the skin, which was not particularly increased in the folds of the skin. Examination of the heart was negative except for a rather harsh systolic murmur heard over the precordium. The blood pressure was 120 systolic, 70 diastolic, and the aortic second sound was greater than the pulmonic second sound. The lungs showed egophony, with absent tactile fremitus and breath sounds and flatness to percussion over the right base posteriorly beneath the angle of the scapula. The abdomen was distended, tender and doughy. Splenic dullness was increased, but the edge was not felt. There were no masses or shifting dullness. There was no ankle edema. The remainder of the examination was negative.

The temperature was 99.6°F, the pulse 100, and the respirations 22.

Examination of the blood revealed a red-cell count of 3,200,000 with 105 gm of hemoglobin (photoelectric-cell technic), and a white-cell count which varied from 4600 to 6700, with 60 per cent polymorphonuclears, 25 per cent lymphocytes, 11 per cent monocytes, 2 per cent eosinophils and 2 per cent basophils, the smear showed moderate achromia with moderate variation in size and shape, the platelets were normal. A blood Hinton test was negative. The urine examination was negative save for the presence of a ++ test for bile. The stools were light brown, soft, formed and guaiac negative, no amebae were observed. A van den Bergh determination showed 7.2 mg of bilirubin per 100 cc of serum, with a biphasic reaction. A liver function test showed 80 per cent of the dye retained in the serum after one hour. The blood sugar was 84 mg per 100 cc., the serum protein 5.7 gm, and the total cholesterol 191 mg. Widal and *Brucella abortus* agglutination tests were negative. Blood and urine cultures were negative.

Roentgenograms of the chest and abdomen showed that the soft tissues of the abdomen had a hazy appearance, apparently due to ascites. The kidneys, however, were faintly visible and appeared normal. The spleen was moderately enlarged. Lying at the tenth interspace on the right there was an area of calcification measuring 1 cm

in diameter, which probably represented a small gallstone. The right diaphragm was obscured by a hazy homogeneous density in the lower right chest. Fluoroscopically motion of the right diaphragm was limited. The left lung was clear. The heart shadow was transverse in position and appeared to be slightly enlarged. The appearance was consistent with fluid at the right base.

The patient's temperature, pulse and respirations fell to normal the day after admission and remained so for the seven-day hospital stay. The right chest was tapped and bloody fluid obtained, revealing 164,000 red cells and 430 white cells (mostly lymphocytes) per cubic millimeter. A fragility test was normal. The patient improved, although without known cause, and was discharged on the seventh hospital day.

*Third Admission* (six months later). Following discharge the patient had monthly attacks of fever lasting four to five days with temperatures ranging around 103°F, associated with pleural pain under the right or left costal margin. Two months before admission one such episode was associated with loud pericardial friction sounds, following which a rapidly progressive pericardial effusion developed that gradually subsided with Mercupurin medication. Pleural effusion regularly followed each febrile episode and never completely cleared. One month before admission a typical gallstone colic occurred, and a week later she began to complain of diffuse severe headaches. A neurological examination was negative, but a few days later a right homonymous hemianopsia was observed. The fundi were normal, however. A swaying and unsteady gait developed so that she bumped into objects in walking about her home.

Physical examination revealed definite jaundice of the skin and scleras. There was evidence of pleural effusion, but pericardial effusion was not demonstrated. The tip of the spleen was palpated to about the level of the umbilicus, it was tender, firm and smooth. The liver was palpated 8 cm below the costal margin in the right midclavicular line. In the epigastrium just to the right of the midline there was a firm, round, tender mass that had not been observed before. A neurological examination revealed a right homonymous hemianopsia and an unsteady gait with a positive Romberg test. Deep reflexes were stronger on the right than on the left. A lumbar puncture was negative. Roentgenograms of the skull were negative.

The temperature, pulse and respirations were normal.

The patient remained in the hospital for four

days and then was discharged home, without definite improvement.

Two weeks after discharge a lumbar puncture for increasing headaches was performed by her physician. The initial pressure was 300 mm of water and the terminal pressure after the removal of 20 cc of fluid was 160 mm. Following this she had no further headaches. Ascites continued to increase, with but slight diuresis following the administration of Mercupurin. Four weeks after discharge she had an acute upper abdominal pain that lasted for one hour. She showed an increasingly rapid weight loss, in spite of persistent ascites. About five weeks after discharge she awakened one morning with a very severe frontal headache, and twenty minutes later she became irrational and vomited. She became partly comatose and developed rapid respirations, with a pulse of 48 and a blood pressure of 115 systolic, 80 diastolic. She then developed mild generalized convulsions, went into deep coma and expired about eight hours later, approximately nine years after the onset of symptoms.

#### DIFFERENTIAL DIAGNOSIS

**DR. WYMAN RICHARDSON:** This is a very complicated case but I am going to pick out a possible explanation for most of the patient's symptoms. I think if we try to explain all the symptoms we are going to get into difficulty. We can say that at the beginning of the first admission the patient had cirrhosis of the liver, and the subsequent history indicates that for a long period she got along remarkably well. From the second admission on she had increasingly severe symptoms that eventually resulted in death. The symptoms were not clearly infectious in origin, although she had had bouts of fever, and they did involve the brain terminally. It seems to me that these symptoms could best be explained on the basis of a malignant tumor. If you have a patient with cirrhosis and symptoms suggesting malignant tumor you can guess that the patient has a malignant tumor developing in the cirrhotic liver, in other words, a hepatoma.

In the first place, what about the endocrinological symptoms? We have to explain amenorrhea, pigmentation, possibly hypertrichosis, acne and a curious blood-sugar curve. I am no endocrinologist, and I am not going to get caught in any deep water on this subject, but it seems to me very difficult to put all these symptoms together on any one basis. There is not enough evidence to assume that she had a masculinizing tumor or any such syndrome. All we have is amenorrhea and hypertrichosis. If she had a masculinizing tumor we

should expect the mention of changes in the breasts and of a complete shift of the body habitus toward the masculine type. Acne is common at the time of puberty. It may suggest overactivity on the part of the pituitary gland and does go with certain pituitary disorders of a primary nature. If you consider the pigmentation and the hypertrichosis as due to some endocrine disturbance, you might think of the possibility of adrenal tumor. The trouble is that pigmentation is associated with atrophy of the adrenal cortex, whereas hypertrichosis is associated with tumor of the cortex. The amenorrhea and so forth I am not going to try to put together on a primary pituitary basis. We know she had severe underlying systemic disease, probably present for a long time, and it seems better to consider that this patient's endocrine symptoms were due to a secondary disturbance of development of the endocrine glands as a result of profound underlying systemic disease. Now we come to the pigmentation and the striking thing is that it appeared before there was any considerable amount of jaundice. If it was due to liver disease, I should expect it to have been associated with an obstructive jaundice and with a very severe jaundice, and there should have been with it symptoms which the record states that this patient definitely did not have, that is, itching of the skin. The amount of bile in the blood does not seem to be sufficient to account for this severe pigmentation in the skin. Of course, she may have had a mild jaundice over a very long time, and it may conceivably have caused pigmentation of the skin but in such a case, I should think there would have been more pigmentation in the scleras.

If it was not due to jaundice, what was it due to? We have a patient with cirrhosis of the liver and pigmentation and what looks like a diabetic sugar curve, and in spite of the lack of glycosuria I should call it a pigment cirrhosis, in other words hemochromatosis. I have an impression that hemochromatosis is very rare in one sex or the other but I do not remember which so I am all right on this so far. So let us call it pigment cirrhosis and see what happens.

The second admission is very complicated. I think it is better not to try to pick it apart. If we take the bouts of chills and fever and associate them with gallstones and possibly gallstone colic, one could call this Charcot's fever if one wished to that is, a low-grade infection associated with biliary-tract disease. That does not explain the diarrhea. She may well have picked up an enteritis which was purely incidental. She did have a considerable amount of abdominal pain and



cervical tenderness on pelvic examination. We also know she had gonorrheal infection, and it is quite conceivable that she still had some inflammatory disease in the pelvis. The difficult things to explain and the things we have to talk about are the fluid in the chest, which was definitely bloody, and the pericardial effusion with a pericardial friction rub. Bloody fluid in the chest can be due to a pulmonary infarct, but I do not believe it is very common to get a considerable amount of bloody fluid in the chest on that basis. The commonest cause is a malignant tumor of the chest involving the pleura. In this case there was distinct blood, not just blood-tinged fluid. Of course, you can get bloody fluid from an effusion but usually it is not so bloody as this was. The whole picture could be due to infection, and we should perhaps be thinking in terms of tuberculosis. If I start talking about tuberculosis I am going to wander in a circle and rearrange this whole business, so I am going to say that the symptoms were due to malignant tumor involving the pleura and that the pericardial friction rub probably was on the same basis.

I must mention the fact that she had a systolic murmur in the heart, and therefore we have to consider the possibility of vegetative endocarditis and the throwing off of emboli to account for the chills and fever. I mention that so that I shall have spoken of it, but I do not believe that was the situation here, because we have no other evidence of embolic disturbance. The diarrhea I am going to leave alone.

Then we come to the final episode of some lesion involving the brain. Right homonymous hemianopsia — if I remember my anatomy — means a lesion somewhere posterior to the chiasm. She also had ataxia, which suggests the possibility of cerebellar involvement. I am not going to try to localize it closely because I do not see where to put it. There is no reason to suppose it was an abscess. I do not see how we have any reason to suppose it was an embolus. The onset was not sudden, but gradual. I do not believe that an embolus from the heart would have had such a gradual onset as this. Therefore, we are left with tumor, a tumor involving the brain. The liver was enlarged, and there appeared a rather firm mass in the epigastrium that was thought to be in the region of the gall bladder. Whether this was just a distended gall bladder or involvement of the omentum — the patient had had an omentopexy — or whether it was a malignant tumor I do not know, but it did help me to come to the conclusion that very likely this patient had a malignant tumor in the upper abdomen. If the

mass was gall bladder it is rather in favor of tumor as against stone. We have the information that the patient had cirrhosis of the liver, and I am going to say it was hemochromatosis. I believe she had a malignant tumor, probably a primary liver tumor. As for the rest, she may have had low-grade biliary-tract infection and may have had gonorrheal infection of the pelvic organs, and the endocrine symptoms were probably on a secondary basis in a woman who had a severe underlying disease.

#### CLINICAL DIAGNOSES

Cirrhosis of liver, with splenomegaly and ascites  
HepATOMA, with metastases to lungs and brain

#### DR. RICHARDSON'S DIAGNOSES

Pigment cirrhosis of liver (hemochromatosis)  
Primary tumor of the liver (hepatoma), with metastasis to lungs and brain  
Low-grade biliary-tract infection?  
Pelvic inflammatory disease (gonorrheal)?

#### ANATOMICAL DIAGNOSES

Cirrhosis of the liver, toxic type  
Hemochromatosis, early  
HepATOMA, with metastases to lungs  
Ascites  
Pleural effusion  
Operative wound omentopexy

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY. The death of this patient occurred on an occasion when most of the members of the Department of Pathology were attending a meeting of pathologists in another city. The remaining man could not leave the hospital, and as a result, the autopsy was performed by a member of the clinical staff. Here is his report: "I am not much of a pathologist. I did the autopsy at an undertaking room before the body was embalmed. She had a good omentopexy. I cut into the abdomen and found dilated veins around the site of the previous operation. There was a good deal of straw-colored ascitic fluid. The pelvis was grossly negative. The ovaries and tubes appeared normal. Certainly there was no evidence of any pelvic abscess. The liver was considerably enlarged, and the left lobe, which presented in the epigastrium, contained a large mass that was necrotic and adherent to every thing. By the time I got it out it was quite well broken up. The remaining liver was studded with greenish-white hard nodules. Both sides of the chest contained a lot of straw-colored fluid

The pericardium was smooth and glistening and contained no tumor. The heart appeared normal, and I could see no vegetations along the heart valves. The lungs were studded with masses similar to those in the liver. I did not attempt to examine the head. Both kidneys seemed large to me."

Microscopic examination showed that the tumor was a primary liver-cell carcinoma or hepatoma. In the pulmonary metastases the tumor cells were actively secreting bile into dilated canaliculi which were present between them. The liver showed a very marked cirrhosis, and besides pigmentation due to the extreme grade of bile stasis there was some further pigment. A considerable proportion of the pigment reacts with potassium ferrocyanide and is hemosiderin. So we can say there was some degree of hemochromatosis. I find myself skeptical, however, as to whether that was the primary cause of the cirrhosis because, although pigment was present in moderate amounts in the liver cells, there was almost none in the stroma. In a primary hemochromatosis the liver cells, as they die, deliver up this pigment, which is carried by phagocytes to the portal areas and then deposited in large amounts in the stroma. That condition was not present here. I think there was beginning hemochromatosis, but the original cirrhosis was something else and I have no idea what. Sections from the pancreas showed no pigment deposits.

DR. RICHARDSON: Have you a section of the skin?

DR. MALLORY: We did not get any, unfortunately. The degree of hemochromatosis of the liver was slight enough so that I think it is improbable that the skin pigmentation which had been present for eight years, was due to iron, but I can only guess about that.

DR. EDWARD G. THORP: Dr. Chester M. Jones and Dr. William D. Smith saw the patient, and they also thought it was chronic jaundice rather than hemochromatosis that produced the pigmentation.

DR. RICHARDSON: I still think it is funny that she had pigmentation of the skin before she was deeply jaundiced.

DR. THORP: She did have jaundice in the scleras. I saw her during the last three years and the scleras were almost always yellow.

DR. MALLORY: I think we can let Dr. Richardson believe that it was iron pigment in the skin if he wishes to.

DR. RICHARDSON: Thank you.

## CASE 26282

### PRESENTATION OF CASE

*First Admission.* A thirty-nine year-old American salesman was admitted to the hospital complaining of recurrent attacks of red, painful, swollen joints of some ten years duration.

Eighteen years before admission at the age of twenty-one the patient suffered with an acute attack of gonorrheal urethritis which lasted three months and then cleared without residual symptoms. He had led an active healthy life for many years. Although no gourmand, he liked his food on the bountiful rich side; his diet included meat three times a day and he often "sat down to a pound and a half of steak at a time." It was stated that he "used a small amount of wine," never exceeding a quart a week. He took no more than ten glasses of beer a day, and one quart of prohibition-era gin weekly. While thus enjoying himself ten years before admission he had had a recurrence of the gonorrheal urethritis. It lasted only three days, and he received medical attention for it. Shortly after this—the patient did not recall the exact length of time—he was suddenly awakened out of a sound sleep with an excruciatingly painful, throbbing, red and swollen right large toe, the affected area being the metatarsophalangeal joint. He was forced to rest his foot upon a pillow well elevated, and could not bear even the weight of a sheet over the foot. The attack was so severe that he could not sleep for the three days during which the episode lasted. When the attack subsided there was no residual pain, redness or swelling about the joints and there was no limitation of motion or other abnormality. He was well for two years following this attack, and then the same joint of the opposite foot became identically affected for three or four days. Six years before admission a third attack occurred, limited to one toe and at the same time he noted small nodules about the periphery of the pinna of each ear. They were hard, firm, non-tender and not painful. He was able to express a whitish yellow semi-solid material from one of the nodules. He then experienced recurrent attacks of joint pain at more frequent intervals and the joints involved included the metatarsophalangeal joints of the first and fifth digits of both lower extremities, and the wrists. At no time were the shoulders, elbows or knees involved. It was stated that there was no known factor which precipitated the joint attacks; trauma was not incriminated. It was stated that the patient gave a family history of gout. Six months before admission the patient had an at

trick of epigastric pain, a physician was consulted and after x-ray studies a diagnosis of low stomach ulcer was made. The patient was placed on a Sippy regime, and his symptoms were relieved. He continued the diet for five months. Three months before entry and continuing until admission the patient experienced weekly attacks of drenching night sweats. He experienced increasing malaise and weakness and a loss of 12 pounds in weight during the five-month interval before admission. The remaining family, marital and past histories were noncontributory.

Physical examination revealed a well-developed, slightly undernourished man in no apparent distress. There was a small area of dullness posteriorly at the left apex of the chest. The heart was not remarkable, save for a soft, blowing, apical systolic murmur. The blood pressure was 140 systolic, 100 diastolic. There were a few old tophi palpable in the pinna of each ear. The remainder of the examination was negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 4,500,000 with 80 per cent hemoglobin, a white-cell count of 9000 with 81 per cent polymorphonuclears, and a normal smear. Examination of the urine was negative. A urine concentration test showed specific gravities which varied from 1.018 to 1.022. Sputum examinations were negative for acid-fast bacilli. A blood Hinton test was negative, as was a complement fixation test for gonococcal antibodies. The nonprotein nitrogen was 50 mg per 100 cc., the fasting uric acid 5.4 mg., the serum protein 6.1 gm., and the venous-blood nonprotein nitrogen 83 mg. The serum uric acid (Benedict) was 8.9 mg per 100 cc. A prostatic smear showed no gram-negative intracellular diplococci. A phenolsulfonephthalein test of urinary excretion showed 10 per cent excretion in one half hour, and 25 per cent total excretion in one hour.

Intravenous pyelograms showed that the kidney outlines were visible on both sides. They were rather small, particularly that on the left. The secretion of the dye was somewhat slow. At no time were the pelves well outlined. On the left side the pelvis appeared to be of normal size and shape, on the right there seemed to be slight dilatation and blunting of the calyces.

Roentgenograms of the stomach and duodenum showed scar formation in the center of the duodenal cap. The rugae of the stomach appeared slightly enlarged. The chest plate showed that the diaphragm was normal in position. There was a cavity measuring 4 cm in diameter in the right

apical field, with marked mottling extending down to the third rib on this side. There was a similar cavity with a fluid level in the left lower lung field, lying posteriorly. Films of the hands showed slight soft-tissue swelling about the terminal interphalangeal joint of the left middle finger and a small area of calcification of the soft tissues near the terminal interphalangeal joint of the fourth finger on this side, without any evidence of disease in the joints. The films of the feet showed a triangular area of decreased density measuring about 1.5 cm in width at the base of the first phalanx of the great toe on the right.

The patient remained in the hospital for about three weeks and was discharged to a county tuberculosis sanatorium.

*Second Admission* (five months later) The patient was admitted in a state of anxiety which had developed in close time relation with the discovery of pulmonary tuberculosis and the consequent necessity of changing from living at home to a prolonged stay in a sanatorium. At this time the urine concentrated only up to 1008, with a slight trace of albumin and 8 to 10 white blood cells per high-power field in the sediment, the blood pressure was 150 systolic, 115 diastolic. He was given psychotherapy and re-entered the sanatorium for further care of his tuberculosis.

*Third Admission* (twenty months later) The patient was admitted for further study. The chest lesion had improved under sanatorium care. An ophthalmoscopic examination showed marked nicking of the veins but no exudate or hemorrhage in the fundi. The blood pressure was 196 systolic, 132 diastolic. Although he ran a slightly elevated temperature during the early days of his hospital stay, it slowly fell to normal, and he was discharged on the sixteenth day.

*Final Admission* (twenty-two months later) For three to four months before this admission the patient noted increasing anorexia, malaise, weakness, frequent colds and a weight loss of 15 pounds. He had been on a low-purine diet with 1/120 gr of colchicine three times daily, but in spite of this, two days before admission, acute pain without redness or swelling developed in his knees and toes. He began to vomit and retch. Apparently as the result of frequent retching, he developed diffuse abdominal soreness in the epigastrium along the costal margins. He entered the hospital for further treatment.

Physical examination revealed a poorly developed and nourished man who retched violently but failed to vomit food or gastric contents. There was dullness and bronchial breathing at both

apices, but no rales were heard. The chest examination was otherwise negative. Examination of the heart was negative. The abdomen was equally tender in all quadrants, there were no masses. The liver and spleen were not felt. The toes and metatarsal joints of both feet were acutely tender and slightly reddened. No ear topi were observed.

The temperature was 99°F., the pulse 100 and the respirations 20.

Examination of the blood showed a red-cell count of 3,200,000 with 62 per cent hemoglobin and a white-cell count of 10,000 with 86 per cent polymorphonuclears. The urine showed a specific gravity up to 1.005, with a +++ albumin test and an essentially negative sediment. The stools were guaiac negative, and sputums showed no acid fast bacilli. The blood uric acid was 11.1 mg per 100 cc., and the blood chlorides were equivalent to 97.0 cc. of N/10 sodium chloride per liter. The serum nonprotein nitrogen was 135 mg per 100 cc., the serum calcium 7.9 mg., the serum phosphorus 8.8 mg., and the serum phosphatase 61 units. The carbon dioxide combining power of the blood was 12.6 milliequiv per liter.

Röntgenograms of the chest showed multiple areas of density in the right lung, many of which were rather sharply defined. The upper lobe was reduced in size, displacing the trachea and heart shadows to the right. There was a hazy band of density in the left lung field.

The patient continued to fail. A uremic frost appeared on his face, he lapsed into coma and expired on the twelfth hospital day, some fourteen years after the onset of joint symptoms.

#### DIFFERENTIAL DIAGNOSIS

DR. CHARLES L. SHORT: The history of the first admission seems to be a classic story for acute gouty arthritis. With recurrent attacks involving the big-toe joint in a man, with complete clearing between the attacks, I do not believe we need to take the time to consider any other condition in differential diagnosis. The picture certainly does not suggest gonorrheal arthritis, and I think that the gonorrhea is merely an incidental finding although the infection may have precipitated the first attack. The patient was younger than usual for the onset of gouty arthritis, but we have seen a good many patients in the twenties, and even some children. At the end of four years he apparently developed topi in his ears, and we wonder if they were aspirated and the chemical diagnosis of gout established. From then on he had increasingly frequent attacks. The symptoms became more widely distributed, spreading so as to

involve the upper extremities, but even after ten years when he came into the hospital he was apparently still having recurrent acute attacks and was not in the chronic stage with persistent joint changes.

At the time of his first admission he showed definite signs of renal impairment. I do not quite understand the discrepancies in the nonprotein nitrogen, but in any case he had retention of nitrogenous products. He had a diminished phenol sulfonephthalein test, although it is quite true that he showed no abnormalities in the examination of the urine itself and he concentrated quite well. Apparently he had increased blood pressure, although only one reading is given, and only the diastolic pressure was really high. Certainly we can say that the uric acid reading of 8.9 mg per 100 cc in the serum was definitely high, although, in view of his diminished renal function, this is not necessarily significant. I think we have enough to make a diagnosis of gout without this finding, and I am still curious to know whether the topi were ever aspirated at the time of the hospital admission and a definite diagnosis made.

Shortly before this admission we run into two new sets of symptoms, one which from the history sounds very much like that of a duodenal ulcer, and the other like that of some infectious process, with the physical examination suggesting localization in the chest. I think we might show the x-ray films now, as apparently they established the diagnosis.

DR. AUBREY O. HAMPTON: These films were taken on the first and second admissions. The third admission films are not here. This is the one at second examination. There is scarring in the midportion of the left lung and in the entire upper lobe of the right. I do not see any shadows which could be definitely interpreted as cavities. There are a few discrete round nodules in the lung which could be due to tuberculosis or metastatic cancer. But judging from the description of the previous films and looking at these films, I think tuberculosis is the correct diagnosis.

DR. SHORT: Have you the pyelograms or the bone films?

DR. HAMPTON: No.

The apex of the heart is rather blunted and appears to indicate some hypertension without much dilatation.

DR. SHORT: From reading the description of the pyelograms, would you care to commit yourself?

DR. HAMPTON: From reading the description,

I think one kidney is larger than the other and there is a question of clubbing of the calyces on one side. There is not much wrong with the kidneys.

DR SHORT: It could probably all be due to impairment of function?

DR HAMPTON: Yes.

DR SHORT: From the x-ray findings alone we must make the diagnosis of pulmonary tuberculosis with cavity formation, in spite of the fact that the organisms were not recovered. The kidneys seemed to be small by x-ray and showed diminished excretion, which would fit in with the clinical impression of the renal situation.

To summarize thus far, this patient had had gout for ten years, had evidence of renal damage and presumably had an active duodenal ulcer and active pulmonary tuberculosis. The outstanding features in the next two admissions are the facts that his chest disease had apparently improved, that the blood pressure was rising and that he was showing signs of renal failure.

At the age of forty-three he came in for his final admission. The urine showed a poor concentration, and he had a high nonprotein nitrogen. He had acidosis and phosphate retention. He developed anemia and died, with what seems to have been uremia.

In conclusion, from the clinical findings a diagnosis of gout can be made in this patient, although we have not really an unshakable diagnosis in the absence of demonstration of urates in the tissues. I believe that he had pulmonary tuberculosis and a duodenal ulcer and that he died in renal failure, with hypertensive vascular disease. The last does bear a relation to gout, although we do not know the nature of the relation. In this patient there was no hint of previous kidney disease, such as glomerulonephritis or pyelonephritis. I will mention amyloid disease, but I do not believe we have any evidence for that. As to the nature of the renal lesion, I doubt that Dr Mallory will be able to say that these kidneys are characteristic of gout, however, there will probably be urate deposits in them. If my diagnosis is correct, I hope he will discuss the significance of urate deposits in the kidneys in gout as the cause of renal impairment.

DR TRACY B. MALLORY: Dr King would you like to comment?

DR DONALD KING: I thought that the case looked like one of tuberculosis and that we did not have to consider cancer.

DR JOHN TALBOTT: There is one point that is not in the history but should have been. When the patient was in the army in 1917 the doctors

said he had acute Bright's disease. There were no symptoms which accompanied this diagnosis at that time, and we tended to discount it because kidney changes occur so frequently in patients with gout. As to the family history, there is a brother who has developed classic gout within the past year. I think if Dr Thannhauser were discussing this case he would say that this is an example of primary renal disease, with the gout secondary to the renal insufficiency, a theory which I am reluctant to accept. In addition to gout he had three other diseases which required treatment: tuberculosis, psychoneurosis and duodenal ulcer.

#### CLINICAL DIAGNOSES

Gout, acute tophaceous  
Pulmonary tuberculosis, with cavitation  
Nephritis, gouty  
Duodenal ulcer, healed

#### DR SHORT'S DIAGNOSES

Gout  
Pulmonary tuberculosis  
Duodenal ulcer  
Vascular nephritis

#### ANATOMICAL DIAGNOSES

Nephritis, chronic (? type)  
(Uremia)  
Gout, with tophi of ears and fingers, bilateral  
Pericarditis, acute fibrinous  
Pulmonary tuberculosis, bilateral, fibroid  
Tuberculous adenitis, tracheobronchial  
Pleuritis, chronic fibrous, bilateral, apical  
Cardiac hypertrophy, hypertensive type  
Cysts of kidneys, multiple  
Passive congestion of liver  
Arteriosclerosis, coronary and aortic, slight, renal, marked  
Pulmonary edema

#### PATHOLOGICAL DISCUSSION

DR MALLORY: The autopsy showed obvious gout with extensive urate deposits in the joints, also markedly diseased kidneys. The kidney on one side was quite large because of the presence of one big and numerous small cysts, which I think account for the slight deformity of the pelvis. The kidney on the other side weighed only 75 gm, and I suspect that if the cysts had been extracted from the first kidney it would have had about the same weight, perhaps not quite so small but almost. The kidneys showed very extensive vascular changes, with thickening of the intima of the smaller arteries and arterioles and hyaline-

tion of the glomerular tufts, changes which to my mind are entirely indistinguishable from ordinary vascular nephritis. One might begin to think about malignant vascular nephritis, if one believed the two can be separated. There were just a few, not very conspicuous, urate deposits in the kidney, not enough, however, reasonably to blame the rest of the kidney disease on them. Whether this was a primary vascular nephritis, one due to essential hypertension or the end result of an acute glomerulonephritis which he had in 1917, as Dr Talbott suggested, I do not believe I can say. There was nothing special to suggest the last in the autopsy.

The heart was moderately hypertrophied. There was some coronary sclerosis without however a significant degree of narrowing, and there was very extensive and active pulmonary tuberculosis, with involvement of most of the left upper lobe, part of the right upper lobe and part of the right middle lobe.

**DR. FULLER ALBRIGHT:** What is your interpretation of the connection between gout and kidney disease? Is the kidney disease the cause of the gout, or the gout the cause of the kidney disease?

**DR. MALLORY:** I am not willing to generalize on one case.

**DR. SHORT:** Have you examined kidneys in which you thought the renal lesion was due to the urate deposits alone?

**DR. MALLORY:** I have never seen enough urate deposit to make me think it was the cause of renal insufficiency. Such other cases of gout as I have seen have also showed fairly marked vascular nephritis.

**DR. TALBOTT:** During the past three years, we have been particularly interested in the clearance of inulin by gouty patients. Most of our patients have shown some diminution in this function, which is now recognized as an index of glomerular activity. In a recent report\* from our laboratory, 4 of 25 patients showed a marked diminution of inulin clearance and, hence, of glomerular filtration. Each of these 4 patients died within the past year from renal failure rather than from deforming gouty arthritis. Three of the 4 patients were autopsied at this hospital, and the fourth died in a hospital in a neighboring city. I mention these data because I am particularly impressed with the incidence of renal failure in gouty patients, and at the present time we are as much concerned with the status of the kidneys as we are with the condition of the joints.

**DR. BERNARD M. JACOBSON:** I should like to ask Dr Talbott how many frank cases of gouty kidneys that might have led to uremia are recorded in the literature.

**DR. TALBOTT:** I believe that this question is unanswerable. With the gouty patients who have been autopsied in this hospital no definite conclusion could be reached. In each patient the renal changes were distinctive but not specific for any commonly recognized type of nephritis. From the evidence at hand we are forced to conclude that many factors may be responsible for the inciting lesion in gouty kidneys, with the superimposed damage from increased excretion of sodium urate the anatomical picture is a very bizarre one.

\*Coombs, F. S.; Pecora, L. J.; Thorogood, E.; Conzelmann, W. V., and Talbott, J. H.: Renal function in patients with gout. *J. Clin. Investigation* 19:525-533, 1940.

# The New England Journal of Medicine

Formerly the  
Boston Medical and Surgical Journal  
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND  
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE  
ON PUBLICATIONS

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SUBSCRIPTION TERMS \$6.00 per year in advance, postage paid for the United States Canada \$7.04 per year \$8.52 per year for all foreign countries belonging to the Postal Union

MATERIAL for early publication should be received not later than noon on Saturday

THE JOURNAL does not hold itself responsible for statements made by any contributor

COMMUNICATIONS should be addressed to the *New England Journal of Medicine* 8 Fenway Boston Massachusetts

## HARVARD SCHOOL OF DENTAL MEDICINE

BEGINNING in the fall of 1941, Harvard University, aided by very generous grants from the Carnegie Corporation, the Rockefeller Foundation and the Marble Foundation, will inaugurate a new five-year course in dental education with the avowed purpose of giving the future dental graduate a wider and deeper knowledge of medicine and thus a more favorable background for the study of the essential causes of oral disease. This would seem to be a highly desirable proposal.

The profession of dentistry has over a period of years developed reparative procedures to a degree of precision and ingenuity that is admired by all and valuable to many. Yet the real solution of the problem of dental care lies not so much in repair and reconstruction as in the discovery of the

causes of dental disease and the prevention of abnormal conditions. It has been stated on good authority that those dentists now in practice can care for but 20 per cent of the total population. It is very unlikely that the present type of dental care can be so increased as to provide for the remaining 80 per cent, and it would thus seem that without sacrificing the skill and technical expertness attained under the present methods of education such a school as that now proposed by Harvard University could graduate each year a group of broadly trained men with both M.D. and D.M.D. degrees who could undertake, with some degree of success, the solution of the basic problems involved and thereby reduce the need for reparative and reconstructive dentistry. Furthermore, the association of dental and medical students in their basic preclinical and clinical subjects should bring to the medical graduate a knowledge of oral medicine and oral disease that is now, unfortunately, lacking in their training, and to the dentist a knowledge of internal medicine that could be of inestimable value to him.

## NEUROLOGY

NEUROLOGY as a special department of medicine was inaugurated about one hundred years ago by Romberg. He wrote the first textbook and had the first definite department for diseases of the nervous system, other than psychiatric, in a general hospital. The subject evolved slowly through the efforts of the great French neurologist, Charcot, and his associates and subsequently by the work of their English colleagues, Hughlings Jackson and Gowers. Charcot never found time to write a great textbook, although his contributions to the literature of neurology are extensive. They are mostly in the form of clinical lectures as taken down by his students, supplemented by individual papers in neurological and other journals. Hughlings Jackson also wrote innumerable papers, but never put his ideas into a textbook. Gowers, however, in the nineties wrote one of the great textbooks on neurology, far greater than any up to its time and perhaps as great as any that has ever been written. It was a personal textbook, giving his experiences of many years in caring for patients with neurologic dis-

orders. In addition he read widely into the literature of his time. A book of a slightly different character, and more comprehensive, was published by Oppenheim in Berlin in 1894. Known throughout Europe, the book also became a favorite with English speaking physicians, for there was an excellent English translation of the fifth edition by Alexander Bruce, of Edinburgh. These two books have held the field in an undisputed manner up until the present time, although there have been literally hundreds of other books, nothing has ever been written to compare with them. That of Oppenheim was the more scholarly of the two, with extensive reference to the periodical literature. The book, however, was not quite so personal as that written by Gowers, and although it forms an excellent reference book even today, it did not have the fine touch exhibited in the volume by his colleague in London.

Recently there has come to hand another book, a great textbook of neurology, eminently fitted to be classified in the same category as those written by Gowers and Oppenheim. This is the two-volume text by the late Dr S. A. Kinnier Wilson,\* edited and put into final form by his old friend Dr A. Ninian Bruce, the son of the Edinburgh physician who translated the German book by Oppenheim for English speaking students. Wilson, backed by an enormous clinical experience, combined all the fine clarity of thought so observable in Gowers's textbook with the scholarly reference attitude characteristic of Oppenheim's publication. Written in a frank, straightforward manner, Wilson saw fit to separate the wheat from the chaff in his selected list of references and appears not to have missed any contribution of importance in the periodical literature. Moreover, he obviously evaluated every paper, and in instances where he did not approve, although he thought the observation important, he did not hesitate to say so. This attitude is in every way characteristic of the man, for a more honest, straight-thinking individual could not have been encountered. The completeness of his references, moreover, speaks highly for the efficiency with which he examined the literature. Papers of mod-

erate or even minor importance are referred to if there was even one point that appealed to Wilson. All the great names in neurology of the past forty years are mentioned and in addition, one finds innumerable references to men of lesser importance. In completeness this book could hardly be improved upon. Its importance lies, however, not only in its completeness but in the endeavor of the author to evaluate the material and express his opinion in a clear-cut manner.

Like all textbooks of course, it lags a little behind the times. Advances are being made so rapidly in neurology that no textbook could possibly be up to date when it is issued. This book covers the period up to 1937 or thereabouts, but one misses the latest advances, such as the use of potassium in familial periodic paralysis, Prostigmine in myasthenia gravis and Dilantin in epilepsy. Surgical procedures that are now well accepted such as operation for a ruptured intervertebral disk are, naturally, only briefly mentioned. After one reads some of the chapters, however, it seems that perhaps such unavoidable omissions are not so important as they appear to be at first sight.

Wilson carried out the biblical admonition to "hold fast to that which is good," and for this splendid attitude the medical profession owes him a debt of gratitude. He added to the field of medicine a text of fundamental importance, and quite possibly the last book of its type that will ever be written. The subject of neurology is growing so rapidly that one cannot keep a textbook either up to date or, if a complete résumé of recent advances is added with each new edition, within the bounds of two large volumes. As in other branches of medicine, monographs on single subjects will be the books of the future. The work of this great pioneer investigator is possibly the final report on neurology as a whole. No one was better fitted to evaluate the subject than was Wilson.

## MEDICAL EPONYM

### CHEYNE-STOKES BREATHING

In the *Dublin Hospital Reports and Communications in Medicine and Surgery* (2:216-223, 1818), John Cheyne (1777-1836) professor in Dublin reported "A Case of Apoplexy in Which the Fleshy

\*Wilson, S. A. *Kin Neurology*. Edited by A. Ninian Bruce. 2 vol. 1838 pp. London: Edward Arnold & Co., 1940.



Part of the Heart was Converted into Fat" He wrote

For several days his breathing was irregular, it would entirely cease for a quarter of a minute, then it would become perceptible, though very low, then by degrees it became heaving and quick, and then it would gradually cease again this revolution in the state of his breathing occupied about a minute, during which there were about thirty acts of respiration

William Stokes (1804-1878), physician to the Meath Hospital, reported his "Observations on Some Cases of Permanently Slow Pulse" in the *Dublin Quarterly Journal of Medical Science* (2 73-85, 1846) He quoted Cheyne's description of this type of breathing and described a patient of his own who was similarly affected

For more than two months before his death, this singular character of respiration was always present, and so long would the periods of suspension be that his attendants were frequently in doubt whether he was not actually dead Then a very feeble, indeed barely perceptible inspiration would take place, followed by another somewhat stronger, until at length high heaving, and even violent breathing was established which would then subside till the next period of suspension This was frequently a quarter of a minute in duration

R W B

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

RAYMOND S. TITUS, M.D., Secretary  
330 Dartmouth Street  
Boston

#### FATAL PNEUMONIA IN PREGNANCY, COMPLICATED BY MENINGITIS

Mrs. M. B., a thirty-five-year-old primipara, approximately thirty weeks pregnant, was first seen in the office on April 8, 1933. She complained of a pain in the left shoulder and of having had a cold for a few days. The temperature was 99.8°F, and the pulse 100. She was sent into the hospital immediately.

The family history was non-contributory. The patient gave a history of the usual children's diseases, scarlet fever, typhoid fever, and appendicitis at the age of eight without operation, which was followed by jaundice six months later. The tonsils and adenoids had been removed. Catamenia began at thirteen, were regular with a twenty-eight-day cycle and lasted five or six days.

A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

The last normal period had begun on September 20, 1932, making the expected date of confinement June 28.

Physical examination on admission showed a well-developed and well-nourished woman lying in bed, obviously febrile and complaining of pain in the lower left side. The throat showed moderate injection and slight edema. There was no stiffness or rigidity of the neck. Chest expansion was diminished on the left side, and there were rales over the left lower base, extending upward to the lower border of the scapula. The right lung was clear and resonant. The heart was not enlarged, there were no murmurs. The blood pressure was 112 systolic, 60 diastolic. The abdomen was soft. The uterus was enlarged to a size compatible with a pregnancy of seven and a half months, the fetal heart was heard. No rectal or vaginal examinations were done. The extremities were negative. A diagnosis of pneumonia was made, and a medical consultation was immediately held.

The white-cell count was 12,100. A blood culture and the sputum showed Type 4 (Group 4) pneumococci. An x-ray film showed an inflammatory process involving the lower portion of the left lung with a small amount of fluid.

The temperature vacillated from 99 and 103°F for the first four days, the pulse ranged between 90 and 140, and the respirations were 30. On April 13 the temperature came down to normal, rising only to 100°F. It remained normal for the next two days, and it seemed as if she were improving.

On April 16, after having had irregular uterine contractions for forty-eight hours, a female child was born normally. The baby weighed 2 pounds, 13 ounces, and lived twenty-four hours. Following the birth, the patient's temperature rose to 103.2°F but came down to 100 and remained there for the next few days. The white-cell count on April 16 was 32,000.

On the morning of April 18 the temperature was 100°F, and the pulse 90. The patient complained of pain and stiffness in the neck. A positive Kernig sign suggested meningeal involvement. A lumbar puncture was done, which confirmed the diagnosis of meningitis, turbid fluid being found, bacteriological examination showed the presence of pneumococci. That afternoon the temperature rose to 104°F, and the pulse to 130. The patient became rapidly worse, the temperature rising to 106°F, and the pulse to 150, and she expired on April 19.

Autopsy showed bronchopneumonia of the left lung, left empyema, interlobar abscess, mediastinum

nal abscess, acute endocarditis and purulent meningitis

*Comment* Pneumonia in pregnancy must always be looked on as a very serious complication. In 1933 many types of pneumococci now specifically recognized were put in the large group of Type 4, for which there was no serum available. The treatment was symptomatic and supportive. It has never been considered advisable as a therapeutic procedure to induce labor in cases of pneumonia. It was recognized then that not infrequently pregnancy associated with pneumonia might be terminated normally by miscarriage or premature labor because of the prolonged fever and extreme toxemia. In this case the temperature having come down to normal it was hoped that the pregnancy might be saved; however, labor started spontaneously. The delivery was simple and uncomplicated. The extension into the meninges was not looked for and proved to be a fatal complication.

Chemotherapy might well have saved this patient's life. Nowadays it is customary as soon as pneumonia is diagnosed to start sulfapyridine even before the result of typing has been reported. In cases of pregnancy it is considered advisable to give sulfapyridine early and then serum if the type is known to be amenable to serum therapy. Sulfapyridine should only be administered under adequate medical supervision.

This patient's history suggested the possibility of contagion in that she visited a pneumonia patient three days before she developed the disease herself. It is wise to remember that in pregnancy some patients are more susceptible to infectious diseases, and it is best to be extremely conservative in an attempt to avoid infection.

## DEATHS

**DARLING**—ARTHUR E. DARLING, M.D., of Lynn died June 19. He was in his sixty-third year.

Born in Auburn, Maine, his early education was received there. He attended Bates College and received his degree cum laude, from Harvard Medical School in 1906. From 1906 to 1907 he served as house officer at the Lynn Hospital.

Dr Darling was a fellow of the Massachusetts Medical Society and the American Medical Association and was a member of the Lynn Medical Fraternity.

A nephew and a sister-in-law survive him.

**ELLIOT**—HENRY L. ELLIOT, M.D., of Salem died June 27 in Thomaston, Maine. He was in his sixty-seventh year.

Born in Thomaston, Maine, he attended the local schools there and received his degree from Bowdoin Medical School in 1898. He served his internship at the Salem Hospital and was associated with Dr. Hardy Phipper for twelve years before starting private practice.

He became a member of the staff of the Salem Hospital in 1902.

Dr Elliot was a fellow of the Massachusetts Medical Society and the American Medical Association.

A son, a daughter and three brothers survive him.

## MISCELLANY

### MIDDLESEX UNIVERSITY SCHOOL OF MEDICINE

The degree of Doctor of Medicine was conferred on forty-six students of Middlesex University School of Medicine at commencement exercises on June 10 in Waltham. The following seniors received their degrees cum laude: Jacques Yetwin of Elizabeth, New Jersey; B.S. Rutgers University; S.M. University of Chicago; Simon Coren of Boston; Middlesex College; Theodore Echlov of Boston; A.B. Harvard University; Everett Radovsky of Fall River; B.S. Rhode Island State College. Dr Yetwin also received the Sebrink Prize for the student with the highest scholastic record during the four years.

The Committee on Faculty of Middlesex University has announced the appointment of Dr. J. Richard Weissenberg to a full-time teaching position for a term to commence August 15 in the medical school as professor of histology. Dr. Weissenberg is now acting curator of the Department of Microscopic Preparations in the Wistar Institute of Anatomy and Biology where he was appointed a research fellow in 1938. Born in Germany, he received his M.D. from the University of Berlin where he was a member of the staff of the Anatomical Biological Institute from 1906 to 1933. He became privatdozent of anatomy in 1913 and served on the medical faculty of the University of Berlin from 1922 to 1933 as professor of histology and embryology. He came to the United States in 1937 and was appointed visiting professor of cytology at Washington University School of Medicine, where he taught histology until his Wistar appointment. Dr. Weissenberg is the author of a German textbook in embryology and is well known for his achievements in the field of research.

## CORRESPONDENCE

### NAVY MEDICAL CORPS

*To the Editor* Doctors are urgently needed for the United States Navy to bring its permanent medical corps to full peace time strength.

Examinations for appointments as commissioned officers in the Medical Corps are to be held on August 19, 1940, at the Naval Hospital, Chelsea, and various other naval hospitals throughout the country. Applicants for appointment must be male graduates of a Class A medical school, have completed an internship in a recognized hospital, be less than thirty-two years of age at the time they receive their commissions, be citizens of the United States, and be physically and professionally qualified. Professional qualifications must be demonstrated by competitive written oral and practical examinations embracing the subjects of general medicine, general surgery, obstetrics and gynecology, preventive medicine and medical jurisprudence.

The pay including allowances for the newly appointed medical officer is \$2699 per year if he has no dependents and \$3158 per year if he has dependents.

Applications must be completed and received at the Navy Department prior to August 1, 1940, in order to appear for the August 19 examination. Additional informa-

tion may be obtained by addressing a letter to the Bureau of Medicine and Surgery, Navy Department, Washington, D C

JOHN L. NEILSON,  
*Captain, M C, U S Navy,*  
District Medical Officer

Navy Yard,  
Boston

#### DISTRIBUTION OF BOOK ON CANCER TO MASSACHUSETTS PHYSICIANS

*To the Editor* The Massachusetts Department of Public Health, through a grant from the United States Public Health Service, has recently forwarded to all physicians in the State a book, *Cancer A manual for practitioners*, which has been prepared by a group of specialists and edited by Dr Channing C Simmons

The department endeavors to keep its mailing list of physicians up to date, but there is always the possibility that a small number will be omitted due to change of residence Any physician who has not been receiving department literature is requested to communicate with the Division of Adult Hygiene, 100 Nashua Street, so that he may receive a copy of the book on cancer

PAUL J JARMAUH, M D,  
*Commissioner of Public Health*

State House,  
Boston

#### RESTORATION OF LICENSE

*To the Editor* At the meeting of the Board of Registration in Medicine held June 27, there was restored to Dr James B Ryan, 53 Maple Street, Easthampton Massachusetts, his license which had been suspended on June 6 1940

STEPHEN RUSHMORE, M D, *Secretary*  
Board of Registration in Medicine.

State House  
Boston

## REPORTS OF MEETINGS

### BOSTON ORTHOPEDIC CLUB

A regular meeting of the Boston Orthopedic Club was held at the Boston Medical Library on April 8, with Dr Dennis O Connor, of Yale University School of Medicine, speaking on The Orthopedic Aspects of Radium Poisoning

Dr O Connor recounted the history of the luminous watch-dial painters' epidemic from 1924 to 1930, he explained the technic responsible for the poisoning in this country in contrast to that in Europe. At first only the serious and fatal instances of osteomyelitis and anemia were diagnosed but subsequent investigation revealed many more clinical and subclinical cases. The mode of entrance for the radio-active materials appears to be largely by ingestion (Martland), although Drinker and his associates consider inhalation an important source. The change of technic in 1927 prevented many new cases, but some danger still persists. A more recently recognized hazard is that of the mixers of the radio-active elements, who inhale relatively large quantities of the dust. Precautions against this danger are now being taken.

Dr O Connor stated that 90 per cent of the ingested radio-active materials were excreted in three to six days,

and he suggested that the form of the compound, namely the insoluble radium sulfate, explained this rapid depletion and the long period before symptoms occurred in many cases. Although the method of fixation within the body is not certain, Martland has suggested that the active elements are phagocytized and then deposited in the reticuloendothelial system, particularly in the bone marrow. It has been demonstrated that 2 microgm of active material may prove fatal. Some patients exhibited as much as 180 microgm in the body.

The effects of such poisoning may be a local necrosis of bone and a systemic reaction in the bone marrow, consisting first of stimulation, then of overstimulation and finally of exhaustion of the blood-forming functions. The local effect may be lacking in frequently repeated small exposures. The marrow changes result in an initial leukocytosis of moderate degree followed at varying intervals by depression of the erythrocytes and leukocytes and death, usually from anemia or overwhelming infection. A certain number of patients have developed osteogenic sarcoma, presumably as a result of the constant stimulation.

Dr O Connor suggested that oral hygiene may be an important deterrent to the lodging of particles around the teeth, but that there appears to be some constitutional factor in the resistance to radium poisoning. Only about 20 per cent of the exposed watch-factory workers were found to have consistent electroscopic evidence of radio-active substances after being separated from the source of poisoning. Since methods at that time were relatively inadequate, it was believed that others may have felt the effects without showing definite evidence of the presence of such substances in the body.

The speaker cited typical cases, at orthopedic clinics, of radium poisoning with characteristic arthritic complaints some months or years after variable exposure to the active elements. The onset of symptoms was often related to minor trauma, but roentgenograms revealed areas of focal atrophy and necrosis, particularly near the head of the humerus and the neck of the femur. The treatment consisted of general supportive measures and physiotherapy. The diagnosis should be considered in differentiating metastatic carcinoma, chronic osteomyelitis, multiple myeloma and Ewing's tumor.

The discussion was initiated by Dr William T Salter, who discussed certain metabolic aspects of the disease. The radio-active elements behave like other heavy metals in their relation to calcium, and it is conceivable therefore that ammonium chloride, parathormone and tremendous doses of vitamin D might result in mobilization and excretion of these elements. The percentage which can be thus removed is probably negligible, however. Radium is first distributed throughout the tissues but finally concentrates in the bone trabeculae where it stimulates the marrow. It was emphasized that the marrow picture is one of spotty necrosis and compensatory hyperplasia, even when the peripheral blood shows evidence of aplastic anemia. Dr Salter emphasized the early phase of stimulation and leukocytosis, which is similar to that observed in cases of benzol poisoning and is not generally recognized.

Dr Channing C Simmons warned of the dangers of radium water for the treatment of arthritis, and of Thorotrast and similar compounds for visualization of the blood vessels and the reticuloendothelial system. Six patients seen at the Collis P Huntington Hospital were reported, with 3 dying of osteogenic sarcoma and only 1, who had taken radium water, living and well.

Dr Frank R. Ober cited a case of radium poisoning in which death supervened almost twenty years after the

taking of radium water. Original assays reported no demonstrable activity of dangerous proportions in the water.

Professor Robley Evans, of the Massachusetts Institute of Technology reminded the audience of the increasing danger of all sorts of nostrums whose existence is protected by the mere statement of their active content. An other source of such poisoning may be the products of the cyclotron and other high speed particles that have the essential properties of the responsible alpha particles of radium. Another interesting speculation concerns the heirs of those exposed for it is known that rats descended from poisoned parents develop a higher percentage of sarcomas than do controls. In regard to the high percentage of elimination, Dr Evans stated that the insolubility does not appear to be a factor since the soluble radium chloride has the same properties. Furthermore, the jaw is equally affected when the portal of entry is other than oral. Measurements indicate that the thermal energy which is equivalent to the radio-active energy dissipated is less than one millionth of a calorie per hour per gram of bone. This is about 0.25 r per day or less than is absorbed by the usual roentgenologist, in the form of radiation energy. The minimal toxic dose appears to be about 1 microgram, for slightly more than this has proved fatal while somewhat less has not affected clinically several people who have been known to harbor that amount for four to twenty years.

## NOTICES

### ANNOUNCEMENT

CHARLES SPIVA, M.D., announces the removal of his office from 189 Bates Street, New Bedford to 177 Nash Road New Bedford.

### ANNUAL MEETING OF EYE AND EAR SPECIALISTS

The American Academy of Ophthalmology and Otolaryngology will hold its forty-fifth annual convention in Cleveland October 6 to 11 with headquarters at the Hotel Cleveland.

The Academy an organization of more than 2500 specialists in diseases of the eye ear nose and throat, carries on an active program of education for its members. In addition to scientific papers, an elaborate series of courses is presented at each convention to bring the members up to date in their chosen fields. More than a hundred of these teaching lectures will be offered this year.

Immediately following the Academy meeting there will be a Pan-American Congress of Ophthalmology October 11 and 12, which eye specialists from all the Latin American countries are expected to attend.

Additional information to regard to these meetings may be obtained from Dr William P Wherry 1500 Medical Arts Building Omaha.

### SOCIETY MEETINGS AND CONFERENCES

- SEPTEMBER 2-6—American Congress of Physical Therapy Page 862 issue of May 16.
- OCTOBER 6-11—Annual meeting of Eye and Ear Specialists. Notice above.
- OCTOBER 8-11—American Public Health Association Page 655 issue of April 11.
- OCTOBER 11-12—Pan-American Congress of Ophthalmology Page 878, issue of May 23.
- OCTOBER 14-25—1940 Graduate Fellowship of the New York Academy of Medicine. Page 938 issue of May 30.
- DECEMBER 21—American Board of Internal Medicine Page 369 issue of February 29.
- JANUARY 4, 1941—American Board of Obstetrics and Gynecology Page 1064 issue of June 20.
- APRIL 21-25 1941—American College of Physicians. Page 1065 issue of June 20.

### DISTRICT MEDICAL SOCIETY

#### MIDDLESEX NORTH

JULY 31

OCTOBER 30.

## BOOK REVIEWS

*A Treatise on the Surgical Technique of Otorhinolaryngology* Georges Portmann. Collaborators H. Retrouvey J. Despons P. Leduc and G. Martnaud. Translation by Pierre Viole M.D. 4 cloth 675 pp., with 474 illustrations and 2 colored plates. Baltimore William Wood & Co., 1939 \$12.50

This book presents a graphic record of the various surgical techniques in otolaryngology as employed by Professor Portmann in his clinic at Bordeaux.

Each procedure is briefly discussed as to indications, contraindications and preoperative and postoperative treatment. The excellent illustrations are so arranged that the reader occupies the position of the operator, and the step-by-step process of each technic can be easily followed without changing the position of the book.

Several of the procedures shown are little if at all, used in this country for example the opening of the endolymphatic sac for vertigo, the three-stage operation for total laryngectomy and the trans-septal approach to the sphenoid.

As the record of a master surgeon in his field and as the source of much valuable anatomical information this book should find interested readers among all of those who carry out operative procedures in and about the upper air passages and ears.

*The Social Function of Science* J D Bernal F.R.S. 8 cloth, 482 pp. with 2 charts. New York Macmillan Co 1939 \$3.50.

The conclusions reached by Professor Bernal are so striking that even at the risk of warping their meaning some of them must be removed from their context and quoted.

"We now see that though capitalism was essential to the early development of science, giving it, for the first time a practical value, the human importance of science transcends in every way that of capitalism, and indeed the full development of science in the service of humanity is incompatible with the continuance of capitalism." Toward this unique conclusion the author builds up a strong case, indeed through some four hundred closely packed pages thoroughly buttressed with documentary evidence. Tracing first the historical development of science, then the chaotic muddle into which science has fallen as a result of its impacts with nationalism, capitalism and war, he then attempts the most difficult task of all the problem of the re-organization of science to best serve all human needs.

To these ends he would reorganize the training and selecting of young scientists the science curriculums of schools and colleges, the administration and control of research to eliminate the present wasteful inefficiency the publication and dissemination of information, the co-ordination of private and public projects in science. In fact, he would tear down the present outmoded structure of science and build one in keeping with the ideals of social service. In financing such an edifice, however while still retaining for science its vaunted freedom Professor Bernal finds no satisfying answer under capitalism. To reach its full effectiveness, science requires "a society economically organized so that general human welfare

where similar ground is well covered by books and monographs possessed by almost every physician

*Handbook of Bacteriology for Students and Practitioners of Medicine* By Joseph W. Bigger, M.D., Sc.D. (Dublin), F.R.C.P.I., M.R.C.P. (Lond.), D.P.H., M.R.I.A. Fifth edition. 8°, cloth, 466 pp., with 100 illustrations and 5 colored plates. Baltimore: William Wood & Co., 1939. \$4.25

The author originally set himself the task of writing a condensed textbook of bacteriology because of the frequent complaint of students that the majority of texts are too comprehensive for the usual course of three or four months' instruction. In this he has succeeded admirably. The essential and important phases of the entire subject are accurately presented and controversial matter is eliminated. The style is concise and clear. The present edition has brought this rapidly advancing science up to date, without appreciably increasing the length of the book.

This book should make an ideal text for elementary courses in medical bacteriology. It is not adequate as a reference book or text for advanced students, nor was this the intention of the author. It is regrettable that no references are given. The reviewer believes that a few well chosen references are of value in guiding the interested and more ambitious student to additional reading—a habit which should be encouraged.

*Climate and Evolution* By William Diller Matthew. Arranged by Edwin Harris Colbert. Preface by William King Gregory. With critical additions by the author and others and a bibliography of his scientific works by Charles Lewis Camp and Vertress Lawrence VanderHoof. Special Publications of the New York Academy of Sciences, Vol. 1. Second edition, revised and enlarged. 8°, cloth, 223 pp., with 33 illustrations and 5 tables. New York: New York Academy of Sciences, 1939. \$2.00

There is good occasion to rejoice at the appearance of the second edition, revised and enlarged, of Volume 1 in the series of special publications of the New York Academy of Sciences. The task of preparing this new edition was entrusted to Dr. Edwin Harris Colbert of the American Museum of Natural History, who has included many annotations found in Dr. Matthew's personal copy of *Climate and Evolution*. The preface contains, "A Biographical Sketch of William Diller Matthew, 1871–1930," an excerpt from an article in *Science* (1930) from the pen of Dr. William King Gregory. There is also an annotated bibliography of the author, covering twenty-two pages, arranged by Charles Lewis Camp and Vertress Lawrence VanderHoof.

All past and future readers should heed the following words from Dr. Gregory: *Climate and Evolution* is one of those fortunate books that keep themselves alive. It deals with subjects of enduring scientific interest. And in our time all those who realize how fully the present state of the world is determined by its past history will value its clear statement of principles."

*Principles of Development. A text in experimental embryology.* Paul Weiss, Ph.D. 8°, cloth, 601 pp. New York: Henry Holt & Co., 1939. \$5.00

This volume embodies a discussion of problems in the field of experimental embryology. The text contains a critical account of the individual facts rated by the light they shed on these problems and the contributions they have made, or promise to make, toward their solution. The book is divided into four parts. The first, "The Phenomena of Development," considers the topics of growth,

physicochemical changes, differential growth, differentiation, organization and the problems of development. The second, "The Methods of Studying Development," begins with a history of embryological methods, followed by a consideration of descriptive methods, experimental analysis and model experiments. The third, "Principles of Development," sets forth the problems of the initiation of development, preformed organization, progressing organization, gradual determination and the field concept, reintegration, regeneration and malformations. The fourth, "The Development of the Nervous System," discusses neurogenesis and concludes with a discussion of the development of behavior.

This book should prove very useful to teachers and students in the field of the biological sciences.

*Laboratory Manual for Animal Histology* By Clair A. Hannum. 8°, paper, 105 pp., illustrated. Tucson: University of Arizona, 1939. \$1.75

This syllabus contains a simple account of cells, tissues and organs, with directions for studying prepared sections. There are twelve pages given over to a discussion of the techniques for the preparation of tissues. The author gives several useful pedagogical suggestions in the section on microscopical anatomy.

*Tumors of the Hands and Feet* Edited by George T. Pack, B.S., M.D., F.A.C.S. 4°, cloth, 138 pp., with 56 illustrations, and tables. St. Louis: C. V. Mosby Co., 1939. \$3.00

The recognition and treatment of malignant growths present peculiar problems in the different regions of the body where they occur. The author has brought together in this text a complete review of tumors of the hands and feet. The introductory chapter deals with general principles, and it is followed by separate chapters on carcinoma, subungual melanoma, angiomatous tumors, syriomas and tumors that are primary in the bones. These topics are authoritatively handled by the co-authors—Mason, Adair, Oughterson, Tennant, Brunswick, Coley and Higinbotham. A work of this sort is designed more for the specialist than for the general practitioner, but it will serve to clarify the general surgeon's perplexities in conditions which he rarely sees, and to warn him of the dangers of lesions which might otherwise pass unrecognized or which may require more specialized judgment. Altogether, it is a very valuable addition to the literature.

*Pictorial Midwifery. An atlas of midwifery for pupil midwives.* By Sir Comyns Berkeley, M.A., M.C., M.D. (Canada), F.R.C.P. (Lond.), F.R.C.S. (Eng.), Hon. M.M.S.A., F.C.O.G. Third edition. 8°, cloth, 166 pp., with 245 illustrations. Baltimore: Williams & Wilkins Co., 1939. \$3.00

This book is exactly what it professes to be—an illustrated handbook designed to aid the midwife of Great Britain in her knowledge of the anatomy, physiology and pathology of pregnancy, labor and the puerperium. It is obvious that it should be a help to the pupil midwife in course or in preparation for state examinations, and also to the practicing midwife who desires to refresh her memory. The illustrations are well done, and the descriptive matter concise and simple. It is conceivable that the handbook could be useful to the medical student for use in conjunction with his textbook or as a rapid method of review of those subjects in which the information is satisfactorily transmitted by pictures. It also occurs to the reviewer that many of the illustrations would be useful in simplifying the teaching of nurses, as they clearly show what is now attempted in a series of didactic lectures.

# The New England Journal of Medicine

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VOLUME 223

JULY 18, 1940

NUMBER 3

## CYSTOURETHROGRAMS

Roentgen Visualization of the Urethra, Bladder and Prostate

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BOSTON

**A**CCURATE estimation of the size of the obstructing prostate is difficult. Rectal examination alone enables one to feel that portion of the enlarged gland which lies posteriorly but does not necessarily give information regarding tissue which narrows the urethral lumen. Cysto-

lobes. Degrees of intraurethral enlargement of the prostate are best gauged by examination with the panendoscope but such investigations in elderly, debilitated patients are not only unpleasant but carry with them the danger of hemorrhage and infection. A more accurate estimation of the size and character of the obstructing gland, we believe, can be obtained by cystourethrograms than by cystoscopic and rectal examination, with less risk, discomfort and indignity to the patient.

The increasing use of transurethral methods for relieving prostatic obstruction makes necessary a more accurate knowledge of the size of the prostate, since transurethral resection is best suited to glands of moderate size. Prostates weighing over 60 or 70 gm., we believe, are usually best treated by open operation that is, suprapubic or perineal enucleation. Gross overestimation or underestimation of the size of the obstructing prostate has been a common experience with us and others. Any means by which the size and type of obstruction can be more nearly approximated will aid in the selection of the most suitable type of operation.

Roentgen visualization of the urethra, bladder and prostate is of recent development. In 1933 Flocks<sup>1</sup> discussed its advantages and described the technic that we now use. The information obtained by this method has enabled us to judge more accurately the size of the prostate and the type of enlargement, and has made cystoscopic examination with its disagreeable features, unnecessary in many cases of prostatic obstruction. It has helped us select the cases best suited to transurethral removal of the prostate. Cystourethrograms have provided valuable information in many other conditions such as stricture, prostatic abscess and tumors of the pelvis.

The technic of this procedure is not difficult, and the apparatus is simple. The following are necessary: a soft rubber catheter, No. 16 or 18 Fr.,

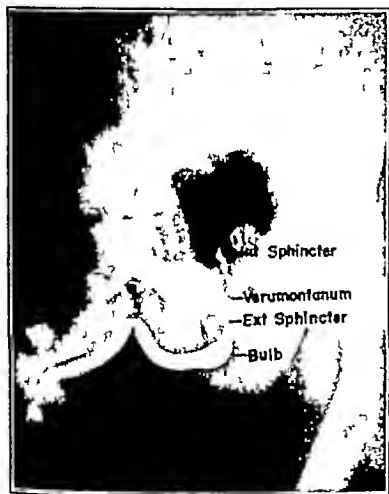


FIGURE 1 Normal Bladder and Urethra (cystourethrogram)

The bladder is outlined by air and the urethra filled with tragacanth Lipiodol emulsion. The verumontanum and external and internal sphincters are outlined.

scopic examination is likewise often misleading for although intravesical protrusions of the prostate can be seen, it is frequently impossible to estimate accurately the size of the obstructing

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FIGURE 2 Case 1 Diverticulum of the Bladder and Fibrous Contraction of the Bladder Outlet Complete urinary retention (sodium iodide cystogram)  
There is a large diverticulum on the right and a small bladder shadow on the left with an irregular, trabeculated wall due to obstruction at the bladder outlet



FIGURE 3 Case 1 Diverticulum of the Bladder and Fibrous Contraction of the Bladder Outlet Complete urinary retention (cystourethrogram)  
The large diverticulum is outlined by air, the small contracted bladder is filled with the emulsion. Note the small bladder neck due to the fibrous contraction frequently associated with diverticula and infection



FIGURE 4 Case 2 Early Benign Hypertrophy of the Prostate (sodium iodide cystogram)  
There is a round, smooth walled bladder without evidence of long standing obstruction. The multiple small calculi that sometimes accompany early hypertrophy of the prostate are evident



FIGURE 5 Case 2 Early Benign Hypertrophy of Prostate (air cystogram)  
The intravesical protrusion of the median lobe of prostate stands out in contrast to the air-filled bladder



FIGURE 6. Case 2 Early Benign Hypertrophy of the Prostate (cystourethrogram)

There is anterior bending of the prostatic urethra characteristic of median-lobe enlargement and a widened shadow of the prostatic urethra due to intraluminal lateral-lobe enlargement compressing the urethra. Transurethral resection was performed with removal of 1 gm of tissue.

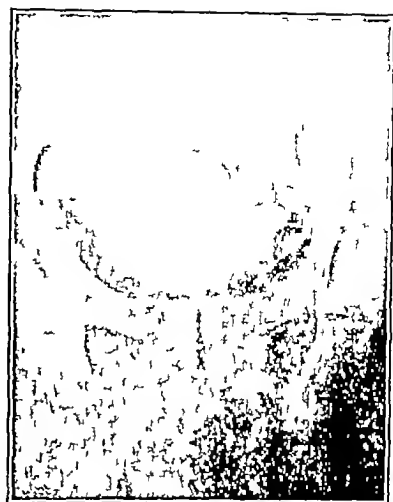


FIGURE 7. Case 3 Benign Hypertrophy of the Prostate (sodium iodide cystogram)

The patient was a seventy-one year-old man with well advanced changes from urinary obstruction. There is an irregular bladder outline due to trabeculation and a reflux up the ureter with an incompetent uretero-vesical valve.



FIGURE 8. Case 3 Benign Hypertrophy of the Prostate (air cystogram)

The large median lobe of the prostate bulges into the bladder cavity.



FIGURE 9. Case 3 Benign Hypertrophy of the Prostate (cystourethrogram)

There is an enlarged median lobe with anterior bending of the urethra and a widened prostatic urethra due to lateral-lobe compression. Transurethral resection was performed.



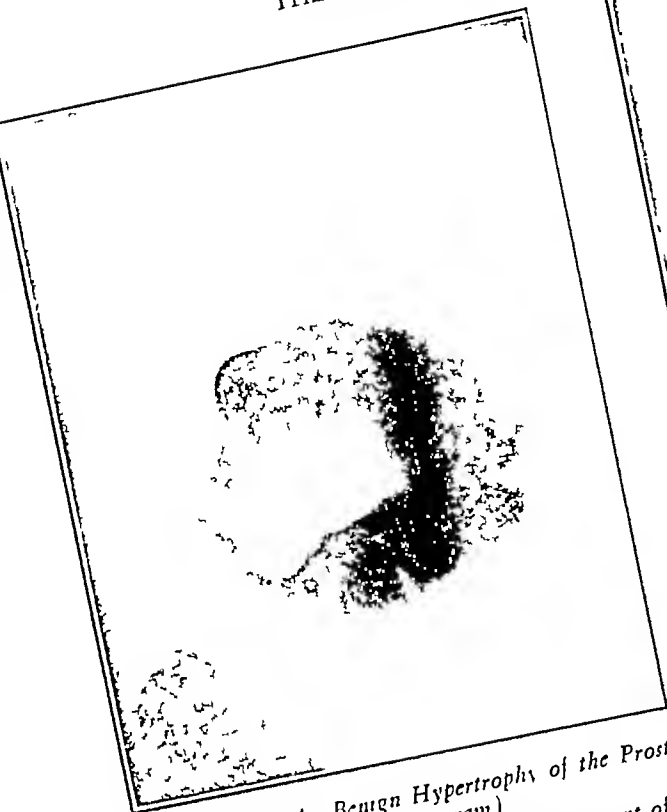


FIGURE 10 Case 4 Benign Hypertrophy of the Prostate (cystourethrogram)

There is well marked intravesical enlargement of the median and lateral lobes — the 'collar type' of hypertrophy — with only slight intraurethral lateral-lobe enlargement. 33.5 gm of tissue were removed by transurethral resection.



FIGURE 11 Case 4 Benign Hypertrophy of the Prostate (cystourethrogram after transurethral resection)  
There is a wide open bladder neck, with complete relief of retention.



FIGURE 12 Case 5 Benign Hypertrophy of the Prostate (cystourethrogram)

This represents the median bar type of obstruction, with some anterior bowing of the urethra and a small filling defect. The retention was relieved by the removal of 3 gm of tissue.



FIGURE 13 Case 6 Benign Hypertrophy of the Prostate (cystourethrogram)

This shows median-lobe enlargement only. There is anterior bowing of the urethra but no spreading to the sides. Note intraurethral lobe enlargement.



FIGURE 14 Case 7 Benign Hypertrophy of the Prostate (cystourethrogram)

There is moderate intravascular enlargement of the median and lateral lobes. 31 gm. of tissue were removed by transurethral resection.

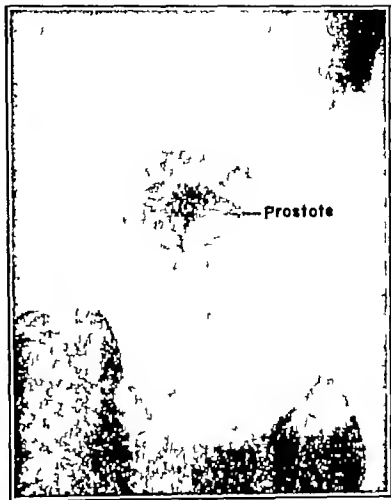


FIGURE 15 Case 8 Benign Hypertrophy of the Prostate (air cystogram)

The enlarged median and lateral lobes protrude into the bladder cavity.



FIGURE 16 Case 8 Benign Hypertrophy of the Prostate (cystourethrogram)

There is marked anterior bowing of the urethra due to the enlarged median lobe with considerable widening of the urethra due to compression by the lateral lobes. From rectal examination and the cystoscopic appearance this prostate was considered too large for resection. The cystourethrogram showed only moderate enlargement; however, and 23 gm. of tissue were removed by transurethral resection with relief of retention.

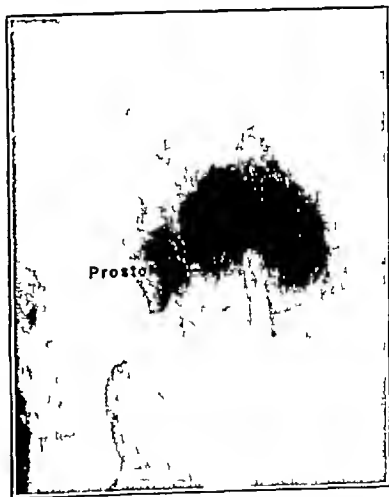


FIGURE 17 Case 9 Carcinoma and Benign Hypertrophy of the Prostate (air cystogram)

There is advanced cancer of the posterior lobe with metastases to the ischium also marked benign intravascular enlargement of the lateral lobes with but little median-lobe hypertrophy.



FIGURE 10 Case 4 Benign Hypertrophy of the Prostate (cystourethrogram)

There is well marked intravesical enlargement of the median and lateral lobes — the collar type of hypertrophy — with only slight intraurethral lateral lobe enlargement. 35 gm of tissue were removed by transurethral resection.



FIGURE 11 Case 4 Benign Hypertrophy of the Prostate (cystourethrogram after transurethral resection)

There is a wide-open bladder neck, with complete relief of retention.



FIGURE 12 Case 5 Benign Hypertrophy of the Prostate (cystourethrogram)

This represents the median-bar type of obstruction, with some anterior bowing of the urethra and a small filling defect. The retention was relieved by the removal of 3 gm of tissue.



FIGURE 13 Case 6 Benign Hypertrophy of the Prostate (cystourethrogram)

This shows median-lobe enlargement only. There is anterior bowing of the urethra but no spreading to denote intraurethral lobe enlargement.

one 50-cc glass syringe, with a 7.5-cm section of catheter securely fastened to the adapter a 90-cc Asepto glass syringe sodium iodide, 3 per cent solution, and a tragacanth Lipiodol emulsion\*

left hand to prevent the escape of the remaining air from the bladder. The 50-cc. glass syringe filled with the emulsion is taken in the right hand and the short length of the urethral catheter

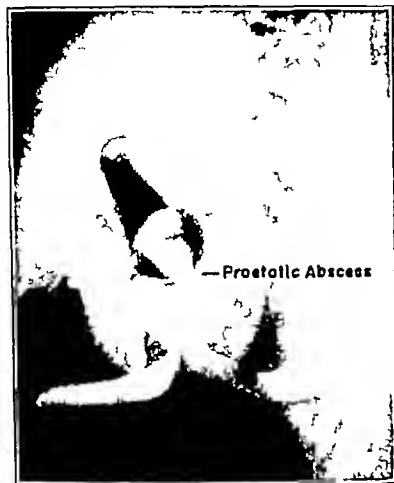


FIGURE 22. Case 13. Tuberculosis of the Prostate (cystourethrogram)

The bladder is small and contracted. There is a large cavity in the prostatic urethra due to an old tuberculous abscess.

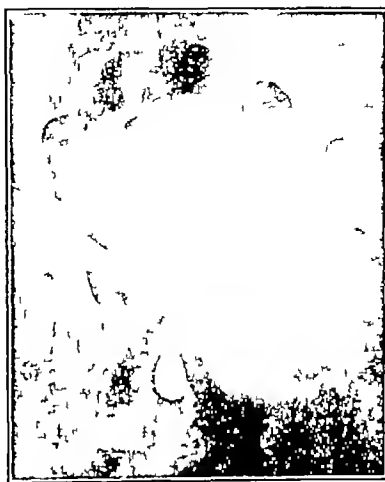


FIGURE 23. Case 14. Chondrosarcoma of the Pelvis (cystourethrogram)

The urethra is distorted and displaced by a huge pelvic tumor.

With the patient on his back on the x-ray table, a plain roentgenogram is taken of the pelvis. A catheter is passed to the bladder, and the amount of residual urine is determined. The bladder is filled to capacity with a 3 per cent solution of sodium iodide, and an anteroposterior exposure is made. The solution is washed out with sterile distilled water. The patient is then turned at a 45° angle with the table, the underneath right leg is flexed and the uppermost left leg extended. The bladder is filled with air through the catheter with the Asepto syringe, and another exposure is taken. About 30 cc. of the air is removed with the syringe and the urethral catheter is withdrawn. At the same time the urethra is closed at the meatus with the thumb and finger of the

left hand to prevent the escape of the remaining air from the bladder. The 50-cc. glass syringe filled with the emulsion is taken in the right hand and the short length of the urethral catheter

is inserted into the urethra. The emulsion is slowly injected, and as the last of it leaves the syringe the final roentgenogram is taken with the patient still in the oblique position. The emulsion is washed out of the bladder, using distilled water injected by the Asepto syringe through the catheter. Four roentgenograms are thus taken. The plain anteroposterior exposure shows the pelvic bones and vesical or prostatic calculi. The picture taken with the bladder filled with sodium iodide solution outlines the bladder wall, defines diverticula, makes evident any regurgitation up the ureters from incompetent ureteral valves and detects the filling defects of large vesical neoplasms. The air cystogram taken in the oblique position affords a contrast for solid tissue projecting into the bladder cavity and very clearly shows intravesical protrusions of the enlarged prostate. The combined cystourethrogram visualizes the entire urethra bladder neck and prostate, and shows the caliber of the anterior urethra and the deformities of the posterior urethra that result from intra-

\*The emulsion is made up as follows.

Powdered gum tragacanth	25 gm.
Ethyl alcohol (95 per cent)	40 cc.
Distilled water	660 cc.

This mixture keeps for two weeks. Two hundred and fifty cubic centimeters of the jelly should be mixed with 60 cc. of Lipiodol. Enough sterile water is added to the mixture to give a consistency equal to that of ordinary lubricating jelly. The emulsion should be kept for use in 50-cc. ampoules. Small sterile glass ampoules.

urethral enlargements of the prostate. The bladder neck is plainly enough outlined to detect the changes due to bars or contractures. The contrast between the air-filled bladder and the lobes of the enlarged prostate, as outlined by the tragacanth-Lipiodol solution, gives a striking picture of the size and character of the obstructing gland.

With a little experience it is easy to interpret the roentgenograms. They illustrate the configuration of the normal urethra and bladder, and the distortions produced by most of the different forms and degrees of prostatic obstruction.

### SUMMARY

Visualization of the urethra, bladder and prostate by cystourethrograms is helpful in estimating the type and degree of prostatic obstruction. It is an aid in the selection of the type of operation best suited to the patient, that is, transurethral removal or open enucleation. In many other conditions it provides valuable information concerning disease of the genitourinary organs.

262 Beacon Street

### REFERENCE

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## VITAMIN A REQUIREMENTS IN RHEUMATOID ARTHRITIS\*

MARSHALL G. HALL, M.D.,† THEODORE B. BAILES, M.D.,‡ AND PHYLLIS SOUTTER§

BOSTON

A GREAT deal of attention has been paid to the diet of the arthritic patient during the past few years. Bauer<sup>1</sup> has suggested that a high-vitamin, high-caloric diet, with adequate amounts of calcium, phosphorus and iron and normal proportions of carbohydrates, proteins and fats, should be the diet of choice for routine use. Despite controversy that is still carried on regarding the amounts of carbohydrate, fat and protein that should be fed to an arthritic patient, there is unanimity of opinion regarding the value of a high-vitamin diet in arthritis.<sup>2</sup>

The identification of certain vitamins by chemical and biological methods has made possible studies concerning the relation of their specific effects to arthritis. No definite deficiency in vitamin B in rheumatoid arthritis has been demonstrated,<sup>3</sup> but Steinberg<sup>4</sup> found that the gastrointestinal symptoms in 105 rheumatoid arthritic patients were alleviated by moderate dosage of vitamin B complex, no effect on the arthritis was noted. Abrams and Bauer<sup>5</sup> believe that in rheumatoid arthritis the usual therapeutic doses of vitamin D will give generally desired results, without the danger and expense of massive dosage. Hall, Durling and Taylor<sup>6</sup> and others<sup>7</sup> showed that 75 per cent of rheumatoid arthritic patients had a subnormal content of vitamin C in the blood. The administration for eight months of a known

satisfactory dose of this substance failed to produce a salutary effect in a large group of patients.

The relation of a low vitamin A level to rheumatoid arthritis has been suggested by Race,<sup>8</sup> who studied the plasma vitamin A and the carotenoid pigments in rheumatic patients by means of the light-extinction density. He found the lowest value given by patients with rheumatoid arthritis.

The present studies were undertaken in order to determine the distribution of vitamin A values among patients with rheumatoid arthritis as compared with normal individuals on a similar dietary regime. At the same time, information was sought as to the daily requirement of vitamin A in the same patients and to determine the effect, if any, on the course of the disease when this requirement was fulfilled.

Direct chemical and spectrographic methods for the determination of vitamin A have been suggested.<sup>9-11</sup> The former cannot be considered to be a specific and quantitative method, and the latter is still in the investigative stage.<sup>10</sup> Bloch<sup>11</sup> first suggested that loss of visual acuity in dim light is related to vitamin A deficiency. Wald<sup>12</sup> has shown that in mammals and other animals vitamin A unites with a protein in the retina to form visual purple. This process takes place continuously and is dependent on a sufficient supply of vitamin A. In addition, this author suggested that the rate of formation of visual purple after the exposure of the retina to bright light is dependent on the available supply of vitamin A.

From the Medical Service of the Robert Breck Brigham Hospital, Boston. The expenses of this investigation were defrayed in part by a grant from the Smith, Kline & French Laboratories, Philadelphia.

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§Volunteer technician.

The increasing ability to see in dim illumination after exposure to bright light has been called dark adaptation, and the measurement of this function has been the basis for methods used for the in direct evaluation of vitamin A deficiency<sup>13 14</sup>

### METHOD

In measuring the dark adaptation curve we have used the biophotometer\* as described by Jeans Blanchard and Zentmire.<sup>15</sup> The satisfactory use of this apparatus in estimating vitamin A deficiency has been confirmed by Jeghers<sup>16</sup> and others.<sup>14</sup>

After an initial period of ten minutes in darkness the subject was exposed to a standardized bright light for three minutes, to exhaust partially the visual purple in the cells of the retina. The dark adaptation curve was then measured and readings were taken every two and a half minutes up to ten minutes following the end of the exposure to bright light. For this study we used the initial reading, taken twenty seconds after the end of the bright light exposure, as an index of the normal or abnormal dark adaptation, and related this reading to vitamin A metabolism.

Seventy nine patients (Group A) with radiological evidence of rheumatoid arthritis in one or more joints or fusiform polyarthritides of over six months duration were utilized. No patient had an obvious focus of infection. For the most part the patients studied were afebrile or had the usual temperature fluctuations—99 to 100°F—found in chronic arthritis. Known gastrointestinal or hepatic dysfunction was absent. Intraocular disease, which would have interfered with the test, was ruled out in every case. Those patients who wore glasses for refractive errors used them in the test. None had received specific vitamin A therapy recently, and the diets varied from the sparse one of the indigent, ambulatory outpatient to the well rounded diet received by the ward patient. The 13 controls were student nurses and hospital attendants and were young adults, all of whom ate the regular hospital diet. For the purpose of determining the incidence of vitamin A deficiency each individual was tested biophotometrically.

By the technic described above, all the controls gave initial biophotometer readings of less than 0.50 millifoot candles. In addition, all patients receiving adequate vitamin A therapy eventually gave and maintained readings under this same figure. For these reasons we have arbitrarily used 0.50 millifoot candles as the upper limit of the normal range.

We were able to study 13 arthritic patients (Group B) for long enough time to determine the amount of vitamin A needed per day to give and maintain normal dark-adaptation curves. These patients were selected from Group A, and all had shown definite abnormal dark adaptation when first tested. They were tested at weekly intervals while receiving increasing supplemental doses of vitamin A (halibut liver oil). Initially, a dose of three capsules (25,500 U.S.P. units) a day was given. This dose was increased by one capsule per day if after two weeks no improvement in the initial reading of the dark adaptation curve had occurred, or if after one week there was a

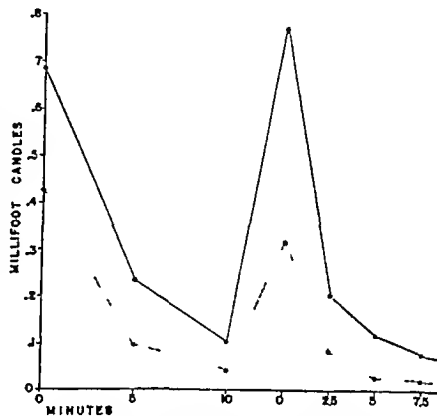


FIGURE 1

The dotted line is the average of the dark-adaptation curves of thirteen controls; the solid line that of seventy nine patients with rheumatoid arthritis.

change in the initial reading to a more abnormal level. This regime was continued until the initial biophotometer reading was maintained at or below 0.50 millifoot candles. In these patients the erythrocytic sedimentation index<sup>17</sup> and the hemoglobin concentration were determined at weekly intervals.

In 45 cases the simultaneous initial biophotometer readings and erythrocytic sedimentation indices were correlated.

### RESULTS

The average initial biophotometer reading of the 79 patients with rheumatoid arthritis was 0.78 millifoot candles and that of the controls was 0.32 millifoot candles. The difference between the average of the curves of dark adaptation for the patients and for the controls is shown in Figure 1.

Twenty-eight (35 per cent) of the 79 patients in Group A had initial readings at or below the normal limit of 0.50 millifoot candles. The same number had initial readings between 0.50 and 1.00 millifoot candles and were considered border-

controls of the same age decade, they are seen to be definitely abnormal (Table 3)

The 30 per cent of the patients who were moderately or severely deficient showed no obvious clinical manifestations of vitamin A deficiency, that is,

TABLE 1 *Average Dark Adaptation Curves of Controls and of 79 Unselected Cases of Rheumatoid Arthritis*

GROUP	No OF CASES	RANGE OF INITIAL BIOPHOTOMETER READINGS	PROBABLE VITAMIN A DEFICIENCY	AVERAGE BIOPHOTOMETER READINGS				
				INITIAL	2½ MIN	5 MIN	7½ MIN	10 MIN
				<i>mft cand</i>	<i>mft cand</i>	<i>mft cand</i>	<i>mft cand</i>	<i>mft cand</i>
Controls	13	0.18-0.47	None	0.32	0.09	0.03	0.02	0.02
Rheumatoid arthritis patients	79	0.13-1.95		0.78	0.21	0.12	0.08	0.05
Subgroup 1	28	0.13-0.47	None	0.35	0.10	0.05	0.02	0.01
Subgroup 2	28	0.55-0.97	Borderline	0.76	0.22	0.12	0.08	0.06
Subgroup 3	17	1.00-1.48	Moderate	1.20	0.27	0.18	0.12	0.07
Subgroup 4	6	1.55-1.95	Severe	1.69	0.38	0.17	0.11	0.08

line or subnormal. Seventeen patients (21 per cent) fell between 1.00 and 1.50 millifoot candles. This we consider a moderate impairment of dark adaptation, indicating moderate vitamin A deficiency. The remaining 6 patients (9 per cent) in Group A

verophthalmia or keratomalacia. Hemeralopia (night blindness) was subjectively noticed by only 1 of the patients. During the test, several complained of nyctalopia, the condition of being more easily dazzled by light than normally.

TABLE 2 *Relation of Age of Rheumatoid Arthritic Patients to Initial Biophotometer Readings*

AGE RANGE	NO OF CASES	AVERAGE INITIAL BIOPHOTOMETER READING
<i>yr</i>		<i>mft cand</i>
10-19	3	0.63
20-29	21	0.63
30-39	14	0.62
40-49	26	0.83
50-59	11	1.05
60-69	4	1.04

had initial readings greater than 1.50 millifoot candles and were considered severely deficient in vitamin A. All but 2 of the patients of these last two sub-groups were receiving the regular hospital diet. The average of the readings of the dark-adaptation curves for the controls and for the 79 patients with rheumatoid arthritis are shown in Table 1. The patients are divided in this table into four groups, as described above, according to the deviation of their initial biophotometer readings from the normal range.

The amount of supplemental vitamin A required to give and maintain initial biophotometer readings of 0.50 millifoot candles or less in the 13 patients in Group B is shown in Table 4. Seven of this group were on the regular hospital diet throughout the experiment, the rest spent part of the time at home. It will be noted that the supplementary doses of vitamin A sufficient to maintain normal readings in these patients ranged from 25,500 to 68,000 U.S.P. units daily.

To illustrate the usual effect of vitamin A therapy the protocol of Case 12 is produced in Figure 2. In addition, it can be seen that while the patient was on a satisfactory maintenance dose of vitamin A (51,000 U.S.P. units) there was an exacerbation of arthritic symptoms, with an increase of the erythrocytic sedimentation index and of the initial biophotometer reading.

In a few patients who were in the quiescent stage of the disease, tests were made after the withdrawal

TABLE 3 *Relation of Dark-Adaptation Curves to Age of Controls and of Rheumatoid Arthritic Patients*

GROUP	No OF CASES	AGE RANGE	AVERAGE BIOPHOTOMETER READINGS				
			INITIAL	2½ MIN	5 MIN	7½ MIN	10 MIN
			<i>mft cand</i>	<i>mft cand</i>	<i>mft cand</i>	<i>mft cand</i>	<i>mft cand</i>
Controls	11	20-29	0.32	0.07	0.03	0.03	0.02
Rheumatoid arthritic patients	21	20-29	0.63	0.16	0.08	0.05	0.03

In Table 2 we have divided the arthritic patients into decades, and it appears that the older age groups had more abnormal initial biophotometer readings. However, when the dark-adaptation values of arthritic patients between the ages of twenty and twenty-nine are compared with those of

of vitamin therapy and a marked fall in the dark-adaptation curve was observed.

Fifteen arthritic patients with erythrocytic sedimentation indices between 0.67 and 1.33 mm per minute demonstrated no apparent relation between this index and the initial biophotometer reading.

However, in all but 3 of 20 patients with indices greater than 1.33 mm the reading ranged from borderline to a severe deficiency. All of 10 patients with indices less than 0.66 mm had normal initial biophotometer readings. The erythrocyte sedimentation

tion<sup>22</sup> Jeghers<sup>22</sup> and others<sup>24, 25, 26</sup> have observed that a vitamin A-deficient but otherwise healthy individual returns to normal in two or three weeks on an intake of 10,000 U.S.P. units of vitamin A per day. The presence of high fever,<sup>5</sup> chronic infec-

TABLE 4 Rheumatoid Arthritic Patients (Group B) Receiving Supplemental Vitamin A

CASE NO.	AGE	SEX	DURATION OF DISEASE	ERYTHROCYTE SEDIMENTATION INDEX RA OR mm /min	INITIAL BIOPHOTOMETER READING BEFORE VITAMIN	AFTER 10 MIN	DURATION OF VITAMIN THERAPY	TYPE OF DIET	FINAL DAILY SUPPLEMENTARY DOSE OF VITAMIN A U.S.P. units
1	23	M	37	1.00-1.70	0.80	0.18	13	Ward	25,500
2	45	P	1	1.05-1.15	0.69	0.44	7	Ward	25,500
3	15	P	1	1.50-2.00	1.68	0.44	14	Ward	34,000
4	29	M	6	0.67-1.10	1.00	0.29	9	Home	34,000
5	47	F	9	0.74-0.98	0.84	0.31	8	Home	34,000
6	41	P	20	1.10-1.80	1.00	0.44	6	Home	44,500
7	48	P	9	0.70-1.00	1.10	0.38	8	Home	42,500
8	32	P	6	0.70-1.05	1.60	0.44	10	Home	51,000
9	43	P	11	1.00-1.85	1.00	0.47	12	Home	51,000
10	27	M	10	0.45-1.50	1.60	0.47	11	Ward	51,000
11	49	M	17	1.50-2.00	0.84	0.44	12	Ward	51,000
12	55	F	1	1.50-2.00	1.50	0.47	17	Ward	59,500
13	54	F	18	0.80-1.65	1.80	0.44	15	Ward	68,000

tation index has been considered the most satisfactory laboratory test aiding in the recognition and evaluation of patients with rheumatoid arthritis,<sup>19</sup> and it appears that this index roughly parallels the initial biophotometer readings in these same patients.

### DISCUSSION

Booher<sup>20</sup> quotes the Technical Commission on Nutrition<sup>21</sup> as recommending 2000 to 4000 units

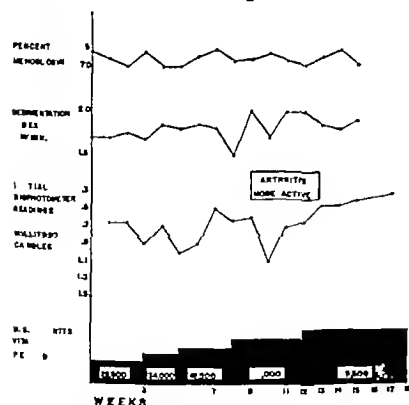


FIGURE 2.

The chart gives the data on a woman (Case 12) aged fifty-five with funiform polyarthritis in all joints of one year's duration. The roentgenographic diagnosis was rheumatoid arthritis.

of vitamin A as the daily requirement for normal adults. The average well-rounded diet contains about 6000 units of vitamin A and is therefore sufficient to maintain normal dark adapta-

tion<sup>6, 27</sup> or cirrhosis of the liver<sup>28</sup> has been shown to diminish the amount of vitamin A or its function in the body.

We have shown in this paper that in rheumatoid arthritis, as in other chronic or infectious diseases, there is an increased demand for vitamin A, as measured by the dark adaptation curve. Also, many arthritic patients require from four to ten times the amount of vitamin A present in their regular diet to maintain normal dark adaptation curves.

There is no means of determining at present whether in these patients this increased need represents an increased utilization, decreased absorption or an inactivation of the vitamin. Until more is known of the mechanism of vitamin A metabolism the normal intake of vitamin A in the patient with rheumatoid arthritis can be measured by the method at hand.

The provision of adequate vitamin A therapy for our patients effected no clinically observable favorable result, but it would be most desirable to eliminate an existing deficiency of this vitamin as a general supportive measure in rheumatoid arthritis.

### SUMMARY

Patients with rheumatoid arthritis showed much higher average dark-adaptation curves than did a group of controls, as measured by the biophotometer. This was found to be true even after age corrections had been introduced.

Sixty-five per cent of a group of 79 rheumatoid arthritics showed abnormal dark adaptation curves. These high readings may be interpreted as an indication of borderline to severe vitamin A deficiency.

Supplemental doses of from 25,500 to 68,000



Twenty-eight (35 per cent) of the 79 patients in Group A had initial readings at or below the normal limit of 0.50 millifoot candles. The same number had initial readings between 0.50 and 1.00 millifoot candles and were considered border-

controls of the same age decade, they are seen to be definitely abnormal (Table 3).

The 30 per cent of the patients who were moderately or severely deficient showed no obvious clinical manifestations of vitamin A deficiency, that is,

TABLE 1 *Average Dark-Adaptation Curves of Controls and of 79 Unselected Cases of Rheumatoid Arthritis*

GROUP	NO. OF CASES	RANGE OF INITIAL BIOPHOTOMETER READINGS mft cand	PROBABLE VITAMIN A DEFICIENCY	AVERAGE BIOPHOTOMETER READINGS				
				INITIAL	2½ MIN	5 MIN	7½ MIN	10 MIN
				mft cand	mft cand	mft cand	mft cand	mft cand
Controls	13	0.18-0.47	None	0.32	0.09	0.03	0.02	0.02
Rheumatoid arthritis patients	79	0.13-1.95		0.78	0.21	0.12	0.08	0.05
Subgroup 1	28	0.13-0.47	None	0.35	0.10	0.05	0.02	0.01
Subgroup 2	28	0.55-0.97	Borderline	0.76	0.22	0.12	0.08	0.06
Subgroup 3	17	1.00-1.48	Moderate	1.20	0.27	0.18	0.12	0.07
Subgroup 4	6	1.55-1.95	Severe	1.69	0.38	0.17	0.11	0.08

line or subnormal. Seventeen patients (21 per cent) fell between 1.00 and 1.50 millifoot candles. Thus we consider a moderate impairment of dark adaptation, indicating moderate vitamin A deficiency. The remaining 6 patients (9 per cent) in Group A

TABLE 2 *Relation of Age of Rheumatoid Arthritic Patients to Initial Biophotometer Readings*

AGE RANGE yr	NO. OF CASES	AVERAGE INITIAL BIOPHOTOMETER READING mft cand
10-19	3	0.63
20-29	21	0.63
30-39	14	0.62
40-49	26	0.83
50-59	11	1.05
60-69	4	1.04

had initial readings greater than 1.50 millifoot candles and were considered severely deficient in vitamin A. All but 2 of the patients of these last two subgroups were receiving the regular hospital diet. The average of the readings of the dark-adaptation curves for the controls and for the 79 patients with rheumatoid arthritis are shown in Table 1. The patients are divided in this table into four groups, as described above, according to the deviation of their initial biophotometer readings from the normal range.

TABLE 3 *Relation of Dark-Adaptation Curves to Age of Controls and of Rheumatoid Arthritic Patients*

GROUP	NO. OF CASES	AGE RANGE yr	AVERAGE BIOPHOTOMETER READINGS				
			INITIAL	2½ MIN	5 MIN	7½ MIN	10 MIN
			mft cand	mft cand	mft cand	mft cand	mft cand
Controls	11	20-29	0.32	0.07	0.03	0.03	0.02
Rheumatoid arthritis patients	21	20-29	0.63	0.16	0.08	0.05	0.03

In Table 2 we have divided the arthritic patients into decades, and it appears that the older age groups had more abnormal initial biophotometer readings. However, when the dark-adaptation values of arthritic patients between the ages of twenty and twenty-nine are compared with those of

xerophthalmia or keratomalacia. Hemeralopia (night blindness) was subjectively noticed by only 1 of the patients. During the test, several complained of nyctalopia, the condition of being more easily dazzled by light than normally.

The amount of supplemental vitamin A required to give and maintain initial biophotometer readings of 0.50 millifoot candles or less in the 13 patients in Group B is shown in Table 4. Seven of this group were on the regular hospital diet throughout the experiment, the rest spent part of the time at home. It will be noted that the supplementary doses of vitamin A sufficient to maintain normal readings in these patients ranged from 25,500 to 68,000 U.S.P. units daily.

To illustrate the usual effect of vitamin A therapy the protocol of Case 12 is produced in Figure 2. In addition, it can be seen that while the patient was on a satisfactory maintenance dose of vitamin A (51,000 U.S.P. units) there was an exacerbation of arthritic symptoms, with an increase of the erythrocytic sedimentation index and of the initial biophotometer reading.

In a few patients who were in the quiescent stage of the disease, tests were made after the withdrawal

of vitamin therapy and a marked fall in the dark-adaptation curve was observed.

Fifteen arthritic patients with erythrocytic sedimentation indices between 0.67 and 1.33 mm per minute demonstrated no apparent relation between this index and the initial biophotometer reading.

## AGE DISTRIBUTION

The majority of patients are over forty years of age. The average age in Outerbridge's series was fifty-four, in Cooper's forty-nine. However, patients as young as fifteen, sixteen and eighteen have been reported in the series of Lieber, Stewart and Lund, and Mayo-Robson<sup>11</sup> reports the case of a patient aged thirty years.

## SEX DISTRIBUTION

The disease is commoner in men than in women. In the large series of Lieber, Stewart and Lund there were 139 males and 83 females, a ratio of 5:3.

## ETIOLOGY

Several etiologic factors are mentioned but nothing definite is known concerning them since evaluation is difficult. Chronic irritation is undoubtedly present, resulting from a constant interplay of acid gastric juice and alkaline pancreatic juice.<sup>5</sup>

Cholelithiasis occurs in 12 to 22 per cent of cases of different series. Gallstones occurred in 20 per cent of Outerbridge's 110 cases, and 22 per cent of Cooper's 14 cases. Lieber, Stewart and Lund report an average of 16 per cent. These figures are above the normal expectation, as only 8.8 per cent of 21,522 autopsies at the Philadelphia General Hospital revealed gallstones.<sup>8</sup>

## CLINICAL CONSIDERATIONS

As already noted, the patient is usually in the cancer age. The symptoms and signs are those of obstruction of the common bile and pancreatic

TABLE 1 Frequency of Symptoms and Signs Based on the Figures of Cooper and of Lieber, Stewart and Lund<sup>8</sup>

SYMPTOM OR SIGN	COOPER	LIEBER ET AL.
	%	%
Jaundice	95	94
Abdominal pain	86	59
Weight loss	8	
Anorexia	1	
Vomiting	36	58
Diarrhea	21	
Palpable gall bladder	50	50
Enlarged liver	86	78
Occult blood in stool	82	
Duodenal defect in gastro intestinal series	80	3

ducts, in addition to duodenal ulceration (Table 1). There is usually a history of painless afebrile, fairly constant jaundice, insidious in onset. However, more or less painful jaundice occurs in almost 50 per cent of cases. There may be weight loss, anorexia, vomiting, diarrhea or epigastric distress. McCabe<sup>12</sup> has suggested that in later stages, when the tumor growth becomes large, pain may result from hypermotility of the duodenum. Physical examination reveals jaundice, emaciation and a distended gall bladder, unless previous gall

bladder disease has caused fibrosis and contraction of the gall-bladder wall. Epigastric pain may be related to the finding of cholelithiasis. The liver edge is usually palpable. The usual diagnosis is carcinoma of the pancreas. A diagnosis of carcinoma of the ampulla of Vater can be made definitely only at operation or autopsy.

## TREATMENT

Since this tumor is usually small, produces early symptoms, metastasizes relatively late and, if untouched, kills early, surgery is justifiable. Operability is frequent, but surgical technical difficulties are great. The operative mortality rates vary from 30 to 70 per cent, with a tendency to approach the lower figure in recent years. Hunt and Budd note that the mortality rate of palliative procedures with various biliary anastomoses still approaches 70 per cent, whereas radical extirpation of the tumor with direct implantation of the bile and pancreatic ducts into the duodenum yields a mortality of about 40 per cent. Cohen and Colp report a series of radical extirpation of the tumor with a 43 per cent operative mortality.

Lieber, Stewart and Lund state that the operative mortality with a palliative procedure is 78 per cent (51 cases), and with primary resection of the tumor 30 per cent (57 cases).

Recurrence after radical extirpation of cancer of the ampulla has been frequent. Many patients live less than one year, the average duration of life being two years after the onset of symptoms.

Cures are infrequent. Muller and Rademaker<sup>13</sup> list 7 patients surviving transduodenal resection of ampullar carcinoma after four years. Hunt and Budd add an eighth case. The case reported in this paper is that of a three year cure, the patient being symptom free to the date of writing.

The procedures of choice are transduodenal resection with reimplantation of bile and pancreatic ducts, and Whipple's two-stage procedure. As Cooper notes:

It is obvious that no single radical procedure is suited to all variations of the disease. If the tumor is small papillary free of ulceration and more or less pedunculated without infiltration at its base, transduodenal resection with reimplantation of the ducts should be the ultimate procedure. If the tumor is ulcerating and infiltrates the duodenal wall transduodenal resection obviously is not the procedure of choice from the viewpoint of permanent cure.

In these cases Whipple<sup>14, 15</sup> advises a two-stage procedure. The first stage includes posterior gastroenterostomy, ligation and section of the common duct below the cystic duct after determining the patency of the cystic duct, leaving a long

slack silk ligature as an indicator on the lower stump of the sectioned common duct, and cholecystojejunostomy. Three or four weeks later the second stage is undertaken, as follows: ligation of the pancreaticoduodenal and gastroduodenal arteries, resection of the descending portion of the duodenum with inversion of the upper and lower ends, and a V-shaped excision of the head of the pancreas and common duct, ligation of the cut ends of the pancreatic ducts and suturing of the two cut surfaces of the pancreas with interrupted fine-silk sutures, and the placing of a cigarette drain in the bed of the resected duodenum.<sup>7</sup> Whipple emphasizes that the mortality is greater with one-stage procedures than with two-stage, that local removal of the growth results in a higher mortality, and that local excision of the ampulla through the duodenum with reimplantation of the common bile duct carries the danger of peritonitis and duodenal fistula.

However, statistics of operative mortality are of relative value only, since a great number of palliative procedures are performed on poor surgical risks. Thus in different series cholecystectomy often has a higher mortality rate than has cholecystectomy, since the former is usually performed only on very ill patients. As Lieber, Stewart and Lund state

The degree of surgery employed in any individual case must depend upon the general condition of the patient, the character and extent of the primary lesion, the presence of extension or metastases and the degree of biliary, pancreatic or duodenal obstruction.

Preoperative preparation includes a high-carbohydrate diet, adequate fluid intake (3000 to 3500 cc daily), infusions of glucose when necessary and blood studies embracing blood-cell counts and the determination of bleeding and clotting times and prothrombin level. Quick's<sup>16</sup> method or modifications thereof may be used to determine the blood prothrombin level. It is wise to feed vitamin K and bile salts regardless of this level, since it is now known that a marked fall in the prothrombin concentration may occur postoperatively. If the level is normal, vitamin K and bile salts are given in the form of 1 Klotogen and 2 Bilein capsules, three times daily. If the prothrombin level is below 80 per cent of normal, larger doses are given (2 Klotogen and 3 Bilein capsules, three times daily) until the prothrombin concentration reaches at least 80 per cent.

Postoperatively vitamin K and bile salts are resumed. Glucose infusions in physiologic saline are given. Since the daily salt requirement averages from 3 to 10 per day, only the first 1500-cc infusion is physiologic saline, the

remaining 1500 to 2500 cc of fluid consisting of 5 per cent glucose in distilled water. Tight abdominal binders are avoided. Transfusions are given as indicated.

### CASE REPORT

L F V (No 45943), a 76-year-old woman, was referred by Dr W Richard Ohler and admitted to the Faulkner Hospital on October 27, 1936. For the previous 2 months she had noted anorexia, occasional nausea with out vomiting and a tendency to constipation. She thought she had lost weight, but was not sure of the amount. Slight jaundice appeared 2 weeks before admission.

The temperature on admission was 98° F, the pulse 80, and the respirations 20. The blood pressure was 155/80. Physical examination revealed a patient in no acute distress but with icteric skin and scleras. The head, neck, heart and lungs were normal. The liver, gall bladder, spleen and kidneys were not palpable. There were no abdominal masses, tenderness or shifting dullness. The urine had a specific gravity of 1.022, it contained the slightest possible trace of albumin and no sugar, and was negative for bile by the foam test. The urinary sediment was negative. The red-cell count was 4,300,000, with a hemoglobin of 84 per cent (Sahli). The white-cell count was 8300, with a normal differential count. The icteric index was 25. The blood nonprotein nitrogen was 30 mg per 100 cc., and the blood sugar 100 mg. A blood Hinton test was negative. Stools were negative for occult blood by the benzidine test on one occasion, and ++ by a guaiac test on a second. An oral Graham test showed no filling of the gall bladder with the dye either before or after the fat meal, and there was no evidence of stone. A gastrointestinal series revealed a normal esophagus, stomach and duodenum, with no gastric retention.

The preoperative diagnosis was carcinoma of the pancreas. Operation was performed by one of us (E L Y) on November 17, 1936. The abdomen was opened, using a right rectus incision. The gall bladder was found to be considerably enlarged, thin walled and without stones, but there were no adhesions. The gall bladder was opened, and a suction tube inserted, with the removal of much thick, ropy bile. The liver was normal to inspection and palpation. The pancreas was soft and normal, except for a small nodule at the head, in the region of the lower end of the common bile duct. The latter was opened. A transverse incision was made into the duodenum, and a tumor of the papilla was found. The nodule was excised, apparently completely. The common bile duct and pancreatic duct were identified, sutured together and then sutured to the wall of the duodenum. The duodenum was closed in two layers. A T tube was placed in the common bile duct. The wound was closed in layers, with a cigarette wick.

The pathological report, by Dr J Beach Hazard, was as follows:

Gross examination shows a roughly oval mass 1.5 by 1.0 by 0.6 cm. The mucosal surface presents centrally a bulging area, 0.6 cm. in diameter and about 0.3 cm. in height, which is gray to pinkish gray, granular and of hard consistence. Centrally there is a slit-like depression, and through this a probe can be passed from the mucosal surface. Surrounding this opening is a narrow margin of soft, gray tissue measuring from 1.0 to 0.3 mm wide. All other surfaces are surfaces of excision and are thus somewhat irregular. The marginal tissue, however, is of soft consistence.

Microscopical examination shows the epithelium of the papilla to be replaced for about two thirds of its extent by atypical epithelial cells forming rather large irregular lumens (Fig 1). Almost the entire duct lining in the section taken is formed by cells of this character. They are roughly columnar and many times form several layers. They extend into the duct wall for a distance of about 3 mm. Only a few mitotic



FIGURE 1 Section through the Papilla of Vater Showing Replacement of the Normal Mucosa by Atypical Epithelium ( $\times 50$ )

ses are found. Tumor is present at the line of excision.

Diagnosis malignant adenoma (adenocarcinoma) growing fairly slowly.

The convalescence was satisfactory but long. There was no distention, sepsis or hemorrhage. Jaundice diminished rapidly. Nausea, vomiting and constipation were the primary postoperative complaints. The intravenous administration of 5 per cent glucose in saline solution was utilized to maintain the fluid and ion balance. In order to rule out intestinal obstruction on the 16th postoperative day a small amount of barium was given by mouth. This revealed evidence of slight delay through the duodenum but no actual obstruction. Nausea and the vomiting became less frequent, and finally ceased, and the patient was discharged on the 25th postoperative day. Annual follow-up studies have revealed an apparent cure, the patient being symptom-free up to December 1939.

#### SUMMARY

Carcinoma of the ampulla of Vater is a relatively rare disease, with a clinical picture of obstruction of the bile and pancreatic ducts.

Incidence based on autopsy statistics is about 0.04 per cent of all necropsies.

Most patients are over forty years of age, and the disease is commoner in men than in women (5/3).

The etiologic factors are unproved, but possible factors are chronic irritation and cholelithiasis.

The important clinical findings are jaundice, abdominal pain, weight loss, anorexia, palpable gall bladder and liver, and occult blood in the stool.

The proper treatment is an early operation whenever the diagnosis is suspected and there are no evident metastases. The procedures of choice are transduodenal excision of the tumor with reimplantation of the common bile and pancreatic ducts, and the two-stage Whipple operation. Operative mortality is high but if untreated the tumor inevitably causes death. At the present time, with the higher mortality of the Whipple procedure, and the lack of any cures, transduodenal resection of the duodenum with reimplantation of the common bile and pancreatic ducts appears to be the procedure of choice with small, completely resectable growths. For the large tumors, however, the Whipple operation should be employed.

The case reported is one of proved ampullar carcinoma, treated by transduodenal resection with reimplantation of the common bile and pancreatic ducts. The patient is alive and symptom free in the fourth year after operation.

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## REPORT ON MEDICAL PROGRESS

## BACTERIOLOGY

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## SULFANILAMIDE THERAPY

ALTHOUGH the introduction of sulfanilamide still remains the most important development for the clinician in the field of infectious disease, little space will be devoted to chemotherapy here, because so much has been written on the subject elsewhere. For the further development of this field it is most important to learn how these drugs act. Two different sets of observations have thrown some light on this problem. First, substances have been isolated from bacteria and tissues which both stimulate bacterial growth and inhibit the action of sulfanilamide.<sup>1-3</sup> *p*-aminobenzoic acid is one such inhibitor that has been identified, and its presence in pus may be the reason why sulfanilamide is so ineffective in abscesses.<sup>4, 5</sup> Presumably, sulfanilamide acts because it is used as an ineffective substitute for the inhibitor by strains that are unable to synthesize *p*-aminobenzoic acid in sufficient amounts when it is absent from the medium. Secondly, oxidation products of sulfanilamide have been found in the blood<sup>6</sup> and urine<sup>7</sup> of treated patients, and in growing cultures<sup>8</sup> that contain sulfanilamide. These products are themselves strong oxidizing agents, producing methemoglobinemia and cyanosis in the patient,<sup>6</sup> and it is postulated that they inactivate certain bacterial enzymes that are highly sensitive to oxidation.<sup>8, 9</sup> There is not as yet enough evidence at hand to reconcile these two lines of investigation.

## SYPHILIS

In these days no review would be complete without a reference to syphilis, and three reports deserve mention. Turner<sup>10</sup> has been able to demonstrate definite protective antibodies in the serum of infected rabbits. Mixtures of their serum with syphilitic material injected into the skin of rabbits produced smaller lesions than did mixtures of normal serum with the same material. Eagle<sup>11</sup> has shown that syphilitic blood contains spirochetal antibodies and that absorption with spirochetes will remove both spirochetal and Wassermann antibodies, whereas absorption with the tis-

sue antigen used in the Wassermann reaction removes only its own antibodies, leaving the former intact. This suggests that the Wassermann reaction is due to an antibody that is called forth by an antigen present in the spirochetes themselves, and not by some product of tissue damage. The most interesting development in the therapeutic field has been the massive-dose method which is being tested by a group<sup>12</sup> at Mt Sinai Hospital, New York City. Patients with primary and secondary syphilis are given a continuous intravenous infusion containing an arsenical drug twelve hours a day for five days, and no more treatment thereafter. The results indicate that this is a reasonably safe procedure and quite an effective one. Though the method is not recommended for general use, it has great possibilities if time shows that such cures are lasting.

## INFLUENZA

A great deal of work is being done on influenza in this country and England. Typical swine influenza is caused by combined infection with a filterable virus and the influenza bacillus,<sup>13</sup> but human influenza is caused by the virus alone,<sup>14</sup> although its worst complications and mortality were due to secondary bacterial invaders in the great pandemic of 1919. Immunity can be produced by an intracutaneous or subcutaneous injection of live virus.<sup>15</sup> This is harmless to the individual, but when tried in swine started several epidemics due to the discharge of virus from the nose.<sup>16</sup> The duration of immunity is relatively short. Various forms of inactivated virus seem capable of inducing immunity in laboratory animals,<sup>17, 18</sup> but until the immunological relation between various strains of virus is worked out for human beings, prophylactic vaccination on a large scale will not be feasible. It is quite possible that none of the present strains of virus would protect against a strain causing a new pandemic.<sup>19</sup>

## UNDULANT FEVER

Undulant fever is a disease that is much talked about but not very often seen in Massachusetts. Recent investigations in areas where brucella infection is prevalent have shown that chronic bru-

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xerosis is far commoner<sup>0-2</sup> than the typical acute disease. The symptoms of this form of infection may be so vague that the patients are considered neurasthenic, and in some cases all the usual laboratory tests are negative.<sup>23</sup> Through the efforts of Huddleson,<sup>4</sup> Poston<sup>25</sup> and others<sup>26</sup> these tests are being constantly improved, but for the practitioner all that is available at present is the agglutination test, blood culture and finally a skin test with a 1:5 dilution of a commercial vaccine. In the agglutination test and skin test the bovine variety of *Brucella abortus* is generally used because it is commoner than the caprine or porcine variety, but actually any one of the three varieties may be used because of the close antigenic relations in this group. A great deal of work will be necessary before we can evaluate the proper significance of these tests in relation to vague symptoms of ill health in a given individual. Certainly no one would suggest that flat feet were due to tuberculosis merely because the patient happened to have a positive tuberculin test, and like tuberculosis, brucellosis has been shown to be remarkably widespread in this country, both in man and in domestic animals.<sup>28-33</sup>

### GNORRHEA

Gonorrhea has begun to receive the attention it deserves as one of mankind's commonest afflictions. The improved methods of culture for this fastidious micro-organism have made its isolation relatively simple. Essentially successful cultivation depends on a medium rich in proteins, adequate moisture, slightly increased carbon dioxide tension and careful temperature regulation. A dehydrated chocolate agar is now on the market which fulfills the first two conditions when fresh. Incubation of the plates in a sealed candle jar, as originally proposed by Nye and Lamb,<sup>34</sup> guarantees sufficient moisture and carbon dioxide. A few strains will grow only at a temperature of 34°C., a few others at 37°C. only but for routine work 35 to 36°C. has been found satisfactory. McLeod and his associates<sup>35</sup> introduced the use of a dye, dimethyl-para phenylene diamine, which is allowed to run across part of the plate after it has been incubated for forty-eight hours. This imparts a pink color to the gonococcal colonies because of the action of an oxydase that they possess,<sup>36</sup> and makes it possible to pick up a few colonies in mixed cultures which otherwise might have been missed. This is particularly valuable in cultures from the uterine cervix. Since the dye test is not absolutely specific, colonies thus identified must be fished and sugars inoculated for final identification. Pitts<sup>37</sup> has recently published

another method which may ultimately prove even better. The importance of good cultural methods is shown by Leahy and Carpenter's<sup>38</sup> figures to the effect that his cultural method, used in conjunction with smears, was 10 per cent more effective than smears alone in detecting cases. Negative cultures have now become one of the most valuable criteria of cure in difficult cases.

The first real advance in the therapy of gonococcal infections came with the study of the thermal death times of strains by Carpenter et al.<sup>41</sup> They found that most strains, particularly those freshly isolated were very susceptible to heat, and were killed in less than five hours at a temperature of 106.7°F. (41.5°C.). This put fever therapy on a rational basis, and the Rochester group, like many others, have secured excellent results in the treatment of resistant cases with artificial fever.<sup>42</sup> In most cases one treatment of five hours at a temperature between 106 and 107°F. is sufficient to effect a complete cure. Treatment must be in the hands of an expert, as it is a rigorous procedure and demands knowledge, judgment and technical skill for its safe administration.

For the ordinary case, chemotherapy remains the method of choice. A few points seem to stand out from the mass of literature on this subject. First, it is best to wait at least a week after onset before administering the drug. Secondly, chemotherapy should produce a marked improvement within several days if dosage is adequate and if the drug is going to be effective. And thirdly, very rigid criteria must be fulfilled after the cessation of treatment if the case is to be considered cured. It has been shown by Westphal, Charles and Carpenter,<sup>43</sup> that gonococci may be made resistant to sulfanilamide or sulfapyridine in vitro by growing the organisms in gradually increasing concentrations of the drug.

### POLIOMYELITIS

It has long been assumed that poliomyelitis is spread by droplet infection, since the only method besides intracerebral inoculation by which monkeys may be regularly infected is the intranasal instillation of virus. Some students of the disease have always opposed this view because epidemics usually occur in late summer and tend to disappear with the first cold weather, like so many insect-borne diseases and enteric infections.

During the past year several investigators<sup>44-46</sup> have successfully demonstrated poliomyelitis virus in the stools of patients and convalescents, and others<sup>47</sup> have shown that it may persist for as long as one hundred and twenty-three days after the illness. In one epidemic several healthy contacts were

also examined and found to excrete the virus in their feces<sup>30</sup>. The fact that the virus was found oftenest in the stools of young children suggests that its presence may have been due to the swallowing of secretions from the nasopharynx. Trask and Paul,<sup>33</sup> however, believe that it is easier to isolate poliomyelitis virus from the stools than from nasal washings, but this may be due to the method employed. The stool itself represents a natural concentrate of a twenty four hour specimen of waste products, and in preparing material for monkey inoculation to test the virus a stool specimen is extracted, the extract concentrated and a large volume injected. This work does not rule out the nasopharynx as the primary source of the virus, but it does show that virus is able to survive in the feces and may be excreted by this route for a very long period of time even after an inapparent infection. Furthermore, Trask and his associates<sup>38</sup> detected poliomyelitis virus in the sewage of two out of three cities with active epidemics in progress, they could obtain it in effluents a half mile below isolation hospitals in which poliomyelitis patients were being treated. This is a striking confirmation of what has long been known in the laboratory, namely that the virus of poliomyelitis is remarkably stable and resistant to chemical manipulations.

As part of this work, Trask, Paul and Vignec<sup>40</sup> attempted to demonstrate the virus in so-called "abortive" cases. Paul, Salinger and Trask<sup>41</sup> had shown that in households where cases of frank poliomyelitis occurred, a number of mild illnesses characterized by malaise, fever, headache, coryza, sore throat, vomiting or diarrhea almost invariably occurred among the other children. From 3 such cases suspected of being nonparalytic poliomyelitis they<sup>40</sup> were able to isolate virus, in 1 case from the nasopharynx and in 2 cases from the stools. This gives more definite proof to the belief that neutralizing antibodies in the serum of most adults are due to very mild infections in childhood, and that paralysis is the exception rather than the rule in this disease. The work of Aycock,<sup>42</sup> who is attempting to show that susceptibility to paralytic poliomyelitis is a hereditary characteristic associated with a certain type of body build and endocrine constitution, is interesting in this connection.

Another question of great interest is whether the virus in human epidemics must enter the nasopharynx or may be transmitted by the bites of insects. Most of our knowledge of poliomyelitis is based on experimental work with laboratory strains that have been passed from monkey to monkey by intracerebral or intranasal inoculation. Many viruses have become fixed by ar-

tificial laboratory manipulation, and thus acquire new and different characteristics when tested in their original host. Trask and Paul<sup>43</sup> attacked this problem and found that recently isolated strains of poliomyelitis virus were often capable of producing infection in monkeys by intracutaneous injection, although the old laboratory strains were strictly neurotropic.

One of the greatest obstacles to large-scale research in this disease has been the fact that man and monkeys are the only susceptible animals. Armstrong<sup>44</sup> recently succeeded in establishing the Lansing strain of virus in the Eastern cotton rat, and he<sup>45</sup> was then able to transfer the disease from these rats to white mice, in which it produced nonfatal paralysis in a large proportion of inoculated animals. Pathologically, the lesions resemble those in monkeys and man, and the virus has retained its virulence for monkeys.<sup>46-47</sup> Unfortunately, this procedure has so far been possible only with this one strain of virus, and many other strains have failed to infect the cotton rat.<sup>48</sup>

In summary, poliomyelitis is a disease which produces many abortive cases and few paralytic ones, and thus most of the population become immune. The virus may be obtained from the nasopharynx and the stools of the abortive cases for several weeks, and may even be detected in sewage contaminated with their feces. The implications of this are clear. Cases of poliomyelitis and any cases of mild vague illness among contacts should be strictly isolated, with the precautions used in the care of both respiratory and enteric diseases. We still do not know how the disease actually spreads, but these facts give some credence to the old idea that poliomyelitis tends to be associated with bathing places, especially rivers and swimming pools. Ellsworth<sup>49</sup> has written an extremely interesting presentation of this point of view.

#### VIRUSES AND IMMUNITY IN TUMORS

Investigations in cancer have followed so many lines that almost every fundamental science can claim the tumor problem as its own. Bacteriology and immunology have a claim which was first staked out by Jensen<sup>50</sup> when he found that mice in which sarcomas failed to grow became resistant to further attempts at tumor implantation. In recent years interest has again been focused on this finding, and the general principle confirmed that in animals with malignant tumors there develops some form of resistance to further attempts to implant that particular tumor in the animal. Andervont<sup>51</sup> showed that if mouse sarcoma was induced in the tails of mice, and

the tails were amputated after several weeks, the animals remained resistant to implantations of this tumor elsewhere. With the Brown Pearce carcinoma of rabbits, Besredka<sup>5</sup> showed that the injection of tumor cells into the skin induced the formation of tumor nodules which regressed and disappeared after a variable time. When they regressed, the animals became immune to intratesticular inoculation, although this led to the induction of rapidly growing metastatic carcinomas in most normal rabbits. This means that the growth of tumor at one site induces a changed reactivity, that is, immunity, to the tumor cells in any other part of the body. Thus, the tumor must either give rise to antigenic material which is absorbed and which produces a general immunity, or else must induce a local production of antibodies which protect the rest of the organism. In order to be antigenic, a tumor must differ chemically in some way from the normal body tissues. It has been suggested that tumor cells themselves differ in their chemical make-up, and support was lent to this theory by Kōgi,<sup>11</sup> who apparently found a high percentage of dextro-rotatory glutamic acid in malignant cells, while normal cells contained only laevo-rotatory glutamic acid. However, this work has not yet been confirmed.

Another theory is that these tumors contain a virus which is the antigenic substance. Virus tumors have been known for a long time and include many common diseases, such as warts in human beings, Rous chicken sarcoma, fowl leukemia and the Shope papilloma and infectious myxomatosis of rabbits. In these diseases the tumor can be transmitted by the injection of a filtrate of ground tumor tissue. When the Shope papilloma virus was discovered in the wild rabbits of the Middle West it was soon noted that virus could usually be found in the papillomas. However if domestic rabbits were inoculated and developed papillomatosis the tumors were much less differentiated than those in wild rabbits, frequently becoming malignant and the virus could never be isolated from them (Kidd<sup>14</sup>). It was evident that virus was present because the rabbits developed neutralizing and complement fixing antibodies for the virus. It has since been found that when wild rabbits develop malignant changes in the papillomas, as they occasionally do, the virus can no longer be demonstrated in the tumors.<sup>15</sup> Kidd came to the conclusion that the virus was masked in these tumors because the disorderly growth led to extravasation of blood into the tumor, and this blood carried sufficient antibody into the tissues to neutralize the virus. In the orderly papillomas of wild rabbits

this extravasation did not occur and there was less absorption of virus into the circulation, and therefore less antibody was present.

With this work in mind, Kidd<sup>14</sup> reinvestigated the Brown Pearce carcinoma. This very malignant tumor more nearly resembles human carcinoma than any other experimental tumor. It is transmissible only by living cells; it takes with regularity only in the testicle; it metastasizes to the regional lymphatics and thence to the internal organs. It arose spontaneously in a syphilitic rabbit seven years ago and has been kept going ever since by rabbit passage.<sup>16</sup> By the same technique he used in the papilloma work, Kidd<sup>17</sup> showed that a saline extract of the fresh tumor tissue contained a substance of high molecular weight, which was similar to the substance obtained from the papillomas and presumably identical with the virus. It was entirely comparable immunologically, since it fixed complement specifically with the sera of rabbits harboring this tumor and no other. However, it differed in that it failed to produce the tumor when injected into the testes of susceptible rabbits. Cheever<sup>18</sup> has confirmed these complement fixation experiments, although his incidence of positive reactions was considerably lower. This work is of great theoretical importance because it represents the first step toward bridging the gap between carcinoma as we see it in man and the virus tumors of animals.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTHEMORTAL AND POSTMORTAL RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 26291

#### PRESENTATION OF CASE

A forty-two-year-old American store clerk was admitted to the hospital complaining of a non-productive cough.

Two years before admission, following a severe cold, the patient developed a nonproductive, brassy cough, which persisted without change until the time of his admission to this hospital. The cough was on occasions made worse by smoking and was occasionally productive, especially in the morning, of small amounts of greenish sputum, which was never blood tinged or malodorous. He noticed no night sweats, orthopnea, dyspnea, or hemoptyses. Save for the cough, he was well until one month before admission when he developed another cold and for several days experienced substernal pain, which was relieved by standing or lying on his side and aggravated by lying on his back. He consulted a physician, and roentgenographic examination of the chest showed a mass in the lower mediastinum. The mass was described as being grapefruit in size and was located near the midline; the lungs were "clear." He was treated in an outside hospital by a series of three x-ray treatments over the mass, but it was stated that it had not decreased in size after a period of several weeks. He was then referred to this hospital for further diagnosis and treatment.

Six years before admission he had suffered an attack of "mild pleurisy" in the left chest accompanying a cold. His weight had always been constant, and his general health good. The remaining family, marital and past histories were non-contributory.

Physical examination revealed a slightly obese man who appeared well. He had an occasional brassy cough. The heart was slightly enlarged, with the apex impulse seen and felt 10 cm. to the left of the sternum, or 2 cm. beyond the midclavicular line in the fifth interspace. The heart sounds were loud and slapping, especially the pulmonic second sound, which was greater than the aortic second sound. The blood pressure was 190 systolic, 120 diastolic. Examination of the lungs showed a patch of increased vocal fremitus, with normal breath sounds and no rales, over the left

lower chest posteriorly in the vicinity of the angle of the scapula. The remainder of the physical examination was negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 5,000,000 with 16.9 gm. of hemoglobin (photoelectric-cell technic), and a white-cell count of 17,200 with 79 per cent polymorphonuclears, a smear was normal. Examination of the urine was negative. No acid fast bacilli were found in the sputum. The serum protein was 6.5 gm. per 100 cc., the blood nonprotein nitrogen 26 mg. A sputum culture showed a moderate number of beta hemolytic streptococci.

Roentgenograms of the chest showed a round mass measuring approximately 10 cm. in diameter in the posterior mediastinum, the center of the mass being opposite the seventh dorsal vertebra. It showed transmitted pulsation. The mass lay slightly more to the left than to the right side and showed no evidence of calcification. Examination including films in the horizontal and upright positions, showed no definite change in the shape of the mass by gravity. It moved markedly upward during the swallowing act. The esophagus was in intimate contact with the mass running along its posterior surface, slightly to the right. The esophagus in this area was markedly flattened being narrow in the anteroposterior direction and wide in the transverse direction. In the profile view the top of the lesion produced a very abrupt change in the course of the esophagus. A definite edge was, however, not visible in the end-on view of the organ. The carina was spread apart by the mass, and the left main bronchus was markedly narrowed. There was a triangular area of marked homogeneous density along the left lower thoracic spine, which extended upward toward the region of the hilus. The heart was slightly displaced to the left but showed no unusual respiratory shift. The lung markings on the left side were slightly less than those on the right. There were a few linear areas of decreased density in the left lower lung field, probably representing localized areas of atelectasis.

On the fifth hospital day an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR. MERRILL SOSNAN \* This indoor sport of differential diagnosis reminds me very much of riding after the fox with a pack of hounds. I

\* Clinical professor of roentgenology, Harvard Medical School; roseologist-in-chief, Peter Bent Brigham Hospital, Boston.

DR. SOSMAN: I have never seen one, but I doubt if it would cause acute angulation of the esophagus from the trachea. Histologic study of the wall of the cyst shows only fibrous connective tissue.

TABLE 1 Data on Five Cases of Mediastinal Cyst

AGE	SEX	SYMPTOM	DURATION	CLINICAL DIAGNOSIS	X-RAY DIAGNOSIS	OPERATION	HISTOLOGICAL FINDINGS	END RESULT
37			37					
33	M	Epigastric pain	15	Tumor of pericardium	Malignant tumor of pericardium	Resection	No epithelial lining	Good
33	M	Pleurisy and cough	6	Mediastinal cyst	Mediastinal cyst	Drainage by marsupialization	Respiratory epithelium	Empyema and draining sinus
67	F	Upper abdominal pain and gas	20	Carcinoma of lung	Carcinoma of lung	Evacuation	No biopsy	—
34	F	Pleurisy	1/12	Mediastinal tumor	Neurofibroma or lymphoma	Resection	Respiratory epithelium	Good
42	M	Cough	2	Mediastinal cyst	Mediastinal cyst	Resection	No epithelial lining	Good

gus That should mean something intrinsic in the wall of the esophagus

CLINICAL DIAGNOSIS

Cyst of mediastinum, bronchiogenic

DR. SOSMAN'S DIAGNOSIS

Leiomyoma or benign cyst arising in the wall of the esophagus (gumma cannot be ruled out)

ANATOMICAL DIAGNOSIS

Congenital cyst of mediastinum

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: I am sorry Dr. Churchill is not here, but I shall read his operative note

The left chest was opened through the bed of the eighth rib. The sixth and seventh ribs were cut between the transverse processes and the angles. The left lower lobe was found to be totally atelectatic. Projecting the lung forward, an incision was made over a cyst which presented between the aorta and the lung. A line of cleavage was found and developed. The cyst was slowly separated from the auricle anteriorly and the esophagus posteriorly. The muscular coat of the esophagus was spread out thinly over the tumor so that over a considerable area it was necessary to expose the undersurface of the mucous membrane. The most adherent part of the cyst was at the carina of the trachea, and it is possible that here was a fibrous cord representing the origin of the cyst. Early in the operation the wall of the cyst was punctured, and cloudy, yellowish fluid containing either fat droplets or cholesterol crystals was evacuated. The wound was closed without drainage.

The cyst was 8 cm. in diameter and contained yellowish mucoid material. The fact that the cyst was attached by a fibrous cord near the carina is very suggestive that it was congenital, forming during fetal life as the result of an imperfect closure of the communication between the trachea and esophagus. Another explanation of its origin is that it was an embryological rest pinched off

There is no respiratory or gastric epithelium, such as may be found in some cases. However, it is quite likely that pressure of the cyst contents had produced atrophy of the epithelium. This case makes the fifth mediastinal cyst that we have had in the past three years. Some of the clinical and pathological findings of these cases are presented in Table 1. It is interesting to note that in the three cases in which a resection was possible the postoperative course was excellent.

CASE 26292

PRESENTATION OF CASE

A fifty-eight-year-old woman was admitted to the hospital complaining of weakness and epigastric gaseous distress.

The patient stated that stomach upsets had troubled her throughout her entire life. Even as a girl she remembered visiting a physician because of indigestion. At the age of thirty years, or twenty-eight years before admission, she suffered an acute attack of epigastric pain, occurring at night, associated with vomiting and loss of appetite, and recurring every day for about two weeks. There were no hematemeses or tarry stools, and the attacks were not associated with hunger or an empty stomach. They were relieved only by hot fomentations applied to the upper abdomen. These attacks of stomach distress, with frequent gaseous eructations, continued at irregular intervals throughout her life. The episodes were not known to have been associated with any food or bowel habits. Approximately six months before admission there appeared to have been a change in symptoms. At that time she experienced increasing weakness, faintness and dizzy spells, during which she felt as though she were going around in circles. This caused her to cease walking alone in the city. Gaseous distention

with frequent belching became more prominent, and she believed that she had passed, on a few occasions at least, tarry or black stools. Ten weeks before admission she arose early one morning to go to the toilet, but as she felt extremely weak and began to perspire profusely she returned to bed, a few hours later she passed a large black stool. She was too weak to sit erect. She was kept in bed for two days. Again a stool was passed which was black, and on examination by her physician it was found to contain blood. She was then admitted to an outside hospital, where she received an immediate blood transfusion and was placed on a milk-and-cream three meal diet. The hemoglobin was found to be 22 per cent the red-cell count 1,800,000. X-ray studies two weeks after admission demonstrated what appeared to be a posterior wall gastric ulcer. Gastric analysis showed no free acid. She remained in bed for three weeks and improved symptomatically. However, on leaving the hospital for the first time she experienced severe, agonizing pain in the lower right mid axillary region, accompanied by or associated with epigastric gaseous distention. Both distention and pain were relieved by belching. After hospital discharge she remained at home and gained weight rapidly, although she stated that she was completely anorexic. There was no vomiting or weight loss during the six week interval before admission. The patient was treated with iron, vitamins, barbitol, and Amphogel (an alumina gel) following each meal. Because the symptoms persisted she was referred to this hospital for further diagnosis and treatment. It was revealed that for many years the patient had experienced attacks of substernal constriction radiating to both arms. These attacks occurred in cold weather when she exerted herself by walking, particularly if she had just eaten a large meal, and were relieved by resting and by belching gas. She never experienced the discomfort in warm weather, and during the two or three years before admission had had no attacks, although her activity had continued about the same. There were no other cardiac symptoms.

The remaining family, marital and past histories were non-contributory.

Physical examination revealed a well-developed and well-nourished woman. The skin, tongue and mucous membranes were pale. Examination of the heart and lungs was negative. The blood pressure was 160 systolic, 90 diastolic. There was a slightly tender, round, apple sized mass in the left central epigastrium, which moved slightly with respiration. The point of attachment could not be determined. There were no other palpable

masses. The liver, spleen and kidneys were not palpated. The nails were spoon shaped, and the hands and lower extremities were normal. Rectal and pelvic examinations were essentially negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 4,600,000 with 65 per cent hemoglobin (Tallqvist), a white-cell count of 5800 with 70 per cent polymorphonuclears, and a microcytic hypochromic smear with marked variation in size, shape and hemoglobin content of the red cells, with many oval and tailed forms, but with no basophilia or nucleated red cells. The urine was negative. Frequent stool examinations were guaiac negative. The gastric analysis showed no free or combined acids either fasting or after alcohol or histamine, the specimens were guaiac positive and one was actually blood streaked.

Röntgenograms of the gastrointestinal tract revealed that the esophagus was normal. In the body of the stomach there was a large, oval, smooth slightly lobulated mass over and around which the barium had to pass before it reached the antrum. The mass was 8 cm long, was slightly movable and was attached to the left curvature of the stomach by a broad base. The pedicle was at least 5 cm in diameter, the upper border being 2.5 cm inferior to the cardiac orifice. The remainder of the stomach contained semi-solid food particles but was otherwise negative. The pylorus opened readily and the barium outlined a normal duodenum. A chest plate and an electrocardiogram were normal.

Endoscopy showed in the body of the stomach, anterior to the gastroscope and somewhat below it as it lay against the posterior wall, a rounded, slightly nodular mass covered by smooth, normal appearing mucosa. The entire tumor could not be well visualized, and although the area of the greater curvature was somewhat obscured by retained secretion the impression was that of a non-ulcerative tumor lying below the mucous membranes and presumably attached along the anterior wall and lesser curvature. There was thickening in the region of the antrum, and peristaltic waves were observed to stop in this region as they approached the pylorus. No ulceration or bleeding was observed.

On the tenth hospital day an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR HELEN S. PITTMAN. May we see the x-ray films?

DR AUBREY O. HAMPTON. I think you can see the mass very easily (Fig 1). It fills most of

the fundic portion of the stomach and is attached along the lesser curvature. It is smooth, and I do not believe you can tell whether the mucosa is intact or not, but in the adjacent stomach wall the mucosal folds are normal. Near the center



FIGURE 1

of the shadow there is an indentation in the tumor outline about 1 cm in diameter that suggests ulceration.

DR PITTMAN: Was there normal peristalsis visible?

DR HAMPTON: There are two waves, not very deep. I think it would have been mentioned in the report if they were abnormal. The stomach does look dilated and rather atonic and does contain secretions or fluid. There is no evidence of previous gastric ulcer.

DR PITTMAN: We have two clear-cut things given to us here—a hypochromic, microcytic anemia and a large tumor of the stomach. Probably the most important thing is the sequence of events in the development of these two conditions. I believe the tumor was benign and had been there for a long time. She had had stomach upsets practically all her life—at least twenty-eight years. It was at the age of thirty that she began to have occasional serious bouts and acute attacks of pain at night with vomiting, relieved by heat, and I am inclined to attribute these to the presence of the polyp or tumor, probably then of smaller size, in the stomach at that time. It seems to be attached too far up for it to have prolapsed through

the pylorus. It is possible that she might have had superficial ulceration at that time, for the pain was more or less like ulcer pain coming on at night. She did have a good deal of vomiting with it, a circumstance which is not suggestive of ulcer.

The next point chronologically happened six months before admission, when there began to be a change in health. She was dizzy and weak—the first indication of blood loss or anemia. Ten weeks before admission she had gross blood loss, she was weak and perspired and soon after passed large black stools, at least twice. She was treated in another hospital on the assumption that she had an ulcer, although at that time it was found she had gastric anacidity. She went home and had very severe agonizing pain in the lower mid axillary region. Whether she could have had intussusception or partial intussusception at that time I am not sure, but I am going to attribute the severe right-sided pain to the presence of the tumor of the stomach.

What about the tumor? I believe that statistically speaking the commonest type of benign gastric tumor, which this certainly was, at least in the beginning, is a myoma. It comprises about 60 per cent of all such tumors. I do not see that we have sufficient evidence from the report to suggest that it had undergone malignant degeneration. It was bleeding, but I think she perfectly well may have had ulceration on the surface of the tumor, or in the surrounding gastric mucosa which had been damaged by the presence of this large tumor in the stomach.

She had achylia, but this may accompany either a benign gastric tumor or hypochromic anemia. It is quite variable with the benign tumors as to whether or not there is significant change in the acidity of the gastric juice. I believe the fibro adenomatous polyps are the ones which are most consistently accompanied by achylia, but statistically, as I have said, the myomas predominate as the benign tumors. Achylia occurs in about 60 per cent of cases of idiopathic hypochromic anemia.

As to the anemia, the underlying factor in hypochromic anemia of the idiopathic type is supposed to be a disturbance of gastric secretion, and she certainly had had plenty of cause for disturbance of the stomach by pressure of this tumor. She could have had this blood picture from bleeding, but I do not believe that I have ever heard of spoon-shaped fingernails following bleeding.

My diagnoses on this individual are that she had a long-standing benign tumor of the stom-

ach—a myoma or a fibroadenomatous polyp—and a microcytic, hypochromic anemia, secondary to long standing gastric disease. The tumor had probably had ulceration in it at some time and may have undergone some malignant change, but there seems to be little evidence for the latter.

DR. THOMAS V. URMY. I can perhaps correct the impression about the gastroscopic examination relative to the peristaltic waves. They did not actually stop at the angulus. They were seen to pass down through the antrum but the antrum seemed distorted by what appeared to be thickening of the wall and the waves were uneven. I got the impression that the wall was infiltrated. You do not often see peristaltic waves above the angulus during that type of examination. It was apparent from what I could see of the tumor that the mucous membrane was for the most part intact. However I could not see the anterior surface because of the position of the gastroscope. There was no generalized gastritis which might explain the hemorrhage, but there had been plenty of time between the previous hospital admission and this one for acute erosions to have healed.

#### CLINICAL DIAGNOSIS

Sarcoma of stomach

#### DR. PITTMAN'S DIAGNOSES

Benign tumor of stomach (myoma or fibroadenoma)

Microcytic hypochromic anemia, secondary to gastric disease.

#### ANATOMICAL DIAGNOSIS

Leiomyoma of the stomach

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY. When this patient was

operated on, the surgeon was rather puzzled by what he found. There was obviously a big tumor filling the cardia. A narrow segment of normal stomach intervened and the entire antrum was markedly thickened, so much so that it felt very much like a scirrhous carcinoma, a linitis plastica of the stomach. The surgeon was afraid to remove merely the obvious tumor, which could easily have been resected since he feared there might be a second malignant process in the pyloric region, so he did a virtually subtotal resection. The antral wall was about 1 cm in thickness, but the thickening proved to be due purely to muscular hypertrophy. There was no tumor in this region, and no significant inflammatory infiltration. The most likely explanation I think is that this tumor of the cardia was sufficiently mobile so that the patient had very numerous and frequent bouts of intussusception with resulting pyloric obstruction and secondary hypertrophy of the antral and pyloric musculature. On the apex of the tumor a shallow erosion was found corresponding in location to the one demonstrated by x-ray. It was very shallow, only a few millimeters in depth and 1 cm in diameter. That is very likely the spot from which the hemorrhages occurred, although she may have had erosions elsewhere which had healed.

Regarding the peristaltic waves, I think a stomach wall as thick as that probably would not work very actively. It would almost impede its own action.

The tumor on microscopic examination was a benign leiomyoma. The sections were absolutely indistinguishable from those of an ordinary fibroid of the uterus, and I think there is no doubt that she had had the tumor at least throughout the whole period of her symptoms and probably even longer.

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## PREMEDICAL EDUCATION

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cisive intention of entering the profession of medicine, it may further be argued, as Mr. Conant has, that guidance by a joint committee from the college and medical school faculties during their remaining three college years might be of great advantage.

It is true that high honor men in the preparatory school and in the freshman year at college will probably continue to do at least creditable and possibly honor work in medical school. From such a group, those who intended to enter medical school could without doubt be chosen with no greater margin of error than now obtains under the system whereby men are selected on the basis of three or four years of college. Such is the case in England and on the Continent, however, certain fundamental differences exist. In England, those who enter the medical profession come almost exclusively from the intellectual and highly educated classes, and British matriculants in medicine, owing to the competitive system of the so-called "public schools," probably have far more factual knowledge and have studied more intensively in their teens than have the majority of their American cousins. In this country, on the other hand, there is a large group of students who, lacking cultural background, are slow to mature intellectually and do not find themselves scholastically until toward the end of their college career. From this group of men come some of America's ablest physicians, and to choose the majority of applicants for medical school at the end of the freshman year would almost certainly exclude a number of excellent men.

The suggestion that a joint committee from the medical school and the college guide those chosen from the freshman class also has its drawbacks as well as its advantages. Theoretically, the man who intends to enter a research career could have his course so planned as to fit him well for his subsequent work, and he who desires to become a practitioner of medicine could have outlined for him a broad educational course, including the minimum requirements in premedical sciences. In actuality, however, it is doubtful whether many freshmen, even if they have decided on a medical

\*Conant, J. B. College education for the future doctor. *Federation Bull.* 25:769-777, 1939.

career, know which of the many branches of medicine they wish to enter. Indeed many fourth year medical students are still uncertain. The special guidance might, therefore, prove to have been along unsuitable lines.

Perhaps a compromise between the old scheme and the new would accomplish the most. Let the medical schools choose from the freshman class a limited number of honor men who are determined to enter medicine and let these few be carefully guided for the next three years. Let the majority of medical students be chosen as heretofore at the end of their college careers.

What college courses should be recommended for the majority? Certainly the minimum premedical science and language requirements should be covered. Without these no man can take full advantage of the present medical curriculums. Beyond this it would seem wise to allow, in fact to urge, each prospective student of medicine to follow his own scholastic bent, regardless of whether his interest lay in history, languages, fine arts or science, such diversification may later prove to be of distinct value in view of the complexity of work in medicine and the variety of opportunity in the medical field. If the student on entrance to college has no specific intellectual interest, it would probably be wise for him to concentrate on the premedical sciences, — chemistry, biology, physics, embryology, comparative anatomy and the like, — for such a man is likely to have scholastic difficulties in medical school and the more time he has spent on purely medical subjects the better he is likely to fare.

## FROZEN FOOD

THE frequency with which home cooking is extolled throughout the land should have long ago brought forth some impelling reasons why it is superior to the sort of cooking we might otherwise expect to find in our restaurants and bake shops. It is apparently just one of those things that is so. The home preservation of food has not been correspondingly free from suspicion, however. It has been scientifically compared with the various commercial processes, usually to its detri-

ment, and has been unable to establish for itself any convincing point of superiority.

There are three primary methods of preserving food to sterilize it by the application of heat, as with the pasteurizing processes, with subsequent protection against infection, to cure it for storage by a salting (canning), drying or smoking process and to inhibit bacterial and fermentive changes by chilling or freezing while still fresh. Technical advantages and disadvantages attach themselves to all these methods.

The development of artificial refrigeration has given a recent stimulus to explore the possibilities of this method. For the best results extremely low temperatures are necessary. Rapid freezing is desirable with many foods in order to prevent the formation of ice crystals which pierce the delicate cell walls, thus causing leakage with consequent change of texture and loss of flavor. Fruit and vegetable cells are more vulnerable in this respect than those of animal products, which are elastic and less easily ruptured. The usual temperature range for rapid freezing is from 0 to -40 F.

A tremendous growth in the frozen food industry has taken place in the past few years. In 1938 the production was close to half a billion pounds. A report by Rose\* summarizes the temperatures, types of process, selection of foods and preservation of nutritive values, and gives fifty odd references to the literature in this field of growing importance. On the basis of this report the Council on Foods of the American Medical Association has voted to give consideration to quick frozen vegetables and fruits with a view to inclusion in the list of accepted foods.

The many advantages of this method of food preservation are dependent on a rather complicated system of transportation and storage, for refrigeration must be maintained throughout, from the original freezing to the purchase by the consumer. This means refrigerated railway cars, trucks, lockers and display cabinets, as well as home facilities provided the food is to be kept for any period of time. Strawberries in December and oysters in July may yet become commonplace!

Rose, M. S. The effect of quick freezing on the nutritive values of foods. J. A. M. A. 114:1336-1361, 1940.



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\*Conant, J. B. College education for the future doctor. *Federation Bull* 25: 269-277, 1939.

VIVIAN—WILLIAM J. VIVIAN, M.D., of Northport, L., New York died June 10. He was in his fifty-ninth year.  
Dr. Vivian received his degree from Dartmouth Medical School in 1912. He was a member of the Massachusetts Medical Society, the American Medical Association, the American Psychiatric Association and the New England Society of Psychiatry.

# ISCELLANY

## BRITISH EMBASSY REGISTERING AMERICAN PHYSICIANS FOR SERVICE WITH GREAT BRITAIN

The British Embassy is registering the names of American physicians who volunteer for service in the United Kingdom in the treatment of casualties so as to have available a list of men who may be called on if the need arises. The statement is made that these men are required mainly for the treatment of civilian casualties and that there is no question of enrolling these men in the medical services of the war forces.

## CORRESPONDENCE

### ARTICLES ACCEPTED BY THE COUNCIL IN PHARMACY AND CHEMISTRY AMERICAN MEDICAL ASSOCIATION

To the Editor: In addition to the articles enumerated in our recent letter the following have been accepted:

#### Abbott Laboratories

- Liver Extract—Abbott (powder) in capsules
- Liver Extract Injectable U.S.P., Abbott, 5 U.S.P. units
- Liver Extract Injectable, U.S.P., Abbott, 10 U.S.P. units

#### Azcol Chemical Co.

- Azcol Ferric Swabs

#### Calco Chemical Co., Inc.

- Sodium Sulfapyridine Monohydrate—Calco

#### Cutter Laboratories

- Pollen Extracts—Cutter (Acacia Alder Alfalfa Alkali Rye Grass Almond Annual Blue Grass Aspen Barley Bent Grass Birch Bract Scalr Bromo Grass Broncho Grass Canada Blue Grass Chapparal Broom Cheat Grass Chrysanthemum Clover Coreopsis Cosmos Cultivated Rye Curly Dock Dahlia Dandelion Date Deodar Cedar Elm English Walnut Eucalyptus False Coastal Ragweed Field Oats Field Wheat Goldenrod Greasewood Hops Incense Cedar Koehlers Grass Locust Mesquite Mexican Tea Monterey Cypress Mountain Sagebrush Mustard Pasture Sagebrush Pecan Perennial Rye Grass Pickleweed Poverty Weed Prairie Sagebrush Privet Quack Grass Rabbit Brush Rose Salt Grass Shasta Daisy Sheep Sorrel Slender Wheat Southern Ragweed Sparscale Spiny Amaranth Squirrel Tail Sugar Beet Sunflower Sweet Vernal Sycamore Tall Oat Grass White Valley Oak Willow Yellow Pine)

#### Endo Products, Inc.

- Ampoules Caffeine with Sodium Benzoate, 2 cc.

#### Lederle Laboratories Inc.

- Staphylococcus Antitoxin Globulin-Lederle Modified

#### National Drug Company

- Diphtheria Toxoid Plain 3 cc. ampul-vial (1 immunization 3 doses, 1 cc. each)
- Diphtheria Toxoid, Plain 15 cc. ampul-vial (5 immunizations, 3 doses 1 cc. each)
- Diphtheria Toxoid Refined Alum Precipitated (1 immunization 2 doses 1 cc. each)
- Diphtheria Toxoid Refined Alum Precipitated (10 immunizations, 2 doses, 1 cc. each)

#### Sharp & Dohme

- Antipneumococcal Serum Concentrated (Pneumococcus Antibody Globulin Types I and II)
- Mulford 20,000-unit package
- Antipneumococcal Serum Concentrated (Pneumococcus Antibody Globulin Types I and II)
- Mulford 50,000-unit package

#### Winthrop Chemical Co. Inc.

- Diodrast Sterile Solution (35 per cent weight/volume) 30 cc.
- Atabrine Dihydrochloride
- Tablets Atabrine Dihydrochloride (Sugar Coated) 0.1 gm. (1½ gr.)
- Tablets Atabrine Dihydrochloride 0.1 gm. (1½ gr.)
- Tablets Atabrine Dihydrochloride 0.05 gm. (¾ gr.)
- Ampoules Atabrine Dihydrochloride Powder 0.2 gm. with ampules, 10-cc. size, sterile distilled water

#### John Wyeth & Brother Inc.

- Silver Pterate Jelly—Wyeth 0.5 per cent
- Soluble Trituration Silver Pterate, 20 per cent with boric acid 80 per cent
- Sulfapyridine—Wyeth
- Tablets Sulfapyridine—Wyeth 0.5 gm. (7½ gr.)

The following articles have been accepted for inclusion in the list of articles and brands accepted by the Council but not described in N.N.R. (*New and Nonofficial Remedies* 1940 p. 560)

#### Endo Products, Inc.

- Ampoules Calcium Chloride Solution—Endo

#### Lakeside Laboratories, Inc.

- Ampules Magnesium Sulfate—Lakeside 25 per cent 2 cc.
- Ampules Magnesium Sulfate—Lakeside 10 per cent 10 cc.
- Ampules Magnesium Sulfate—Lakeside 10 per cent 20 cc.

PAUL NICHIOLAS LEECH, Secretary

535 North Dearborn Street,  
Chicago, Illinois.

## THE "DISCOURAGED STAGE" IN THE CONVALESCENCE FROM INDUSTRIAL INJURIES

To the Editor: Last winter, owing to the hurricane, I had many fallen trees to be cut up and sawed. I happened to have three patients on whom I had operated for rupture of the supraspinatus muscle who were conva-

lescing I employed these men, supervising their work to make sure their shoulders were not overused and letting them take their own time. I paid them only very small wages, but they seemed glad to help me all they could in return for what I had done for them. It was a great pleasure to me to see the rapid improvement in morale, as well as in general physical condition, which took place. They learned that they not only could work again, but that their work was of more value than the payment they received. They knew that they were giving me something. The experiment was so successful that I have decided to try a similar one on a larger scale.

Everyone familiar with the affairs of injured industrial employes will recognize what I mean by the 'discouraged stage' of convalescence following an injury. Almost any patient bears up well when his trouble is acute, for in most cases the acute stage is over in a month and improvement is visible from day to day—certainly is seen from week to week. Often, however, progress is slower. In certain conditions, especially those following injuries to the back, knees and shoulder, improvement may be so slow that it is not recognizable from week to week. It is then that the 'discouraged stage' begins. The loss in morale may be greater than any physical gain. The patients get to think that they will never be able to work again, and worry exaggerates their symptoms. Month by month they lose in general condition, not only from lack of use for their muscles but also from lack of nutrition, if their compensation is not adequate for the size of their families. As such injuries often occur in the later half of life, the age factor looms in this discouragement. Not only do their tissues degenerate more rapidly than in youth, but their optimism also. They need work more than local physiotherapy.

Under modern industrial conditions the jump from idleness to full time work is too abrupt. There should be some opportunity for convalescent employees to "harden up" before resuming their regular trade hours. They should be given opportunity 'to take their own time,' when they first return to work.

My answer to this problem is that in most cases there is almost a whole man to make use of, even if he cannot give full use of the injured part. An employee with an injured shoulder can run errands, carry a pail of water, throw a switch, lift one end of a log, keep accounts and do a hundred other things without abusing his shoulder. And this is true in the case of many other disabilities. Obviously work should be selected which they can do, and this should be the primary consideration of the organizations that employ them.

I therefore propose to organize a business—perhaps better called a therapeutic business—in which I can use convalescents in the 'discouraged stage' at very low wages.

It so happened that the three patients mentioned above presented three different, although in most respects similar, medicoeconomic problems. All three were married men with families of from four to nine children dependent on them for support. The economic differences were that one was a private patient, one a compensation case and the third a charity patient.

The private patient was a laboring man on whom I had operated for rupture of the supraspinatus muscles in both shoulders and obtained good results. After his recovery he got his old job back and worked for me on off days until he had canceled his bill.

The compensation case was that of a painter who had not only torn the supraspinatus muscle but the infraspinatus and teres minor muscles as well. An excellent but

not a perfect result was obtained. The insurance company paid me for his care, and I paid him a small amount for his work. Ultimately the insurance company made a generous settlement with him, as he had shown his willingness to do the best he could with a somewhat impaired arm.

The third patient, a carpenter, was a charity case at a public hospital. An operation restored his ability to work without pain. His family of ten was on relief, and so I paid him a small amount, for although he was not in a condition to do regular work yet he was ready and willing to do anything he could. He grew steadily stronger and by now has done so much for me that I feel he has repaid me for the operation and for the little I have paid him.

Thus in all three cases I have been paid and paid cheerfully. In the second and third cases I have been able partially to pay the patients for their services, also. They all have a realization that they have worked for me for wages that were less than they earned and deserved. I wish to cultivate this realization, for to make them realize that their work is of value is a part of my therapeutics. Before I had operated on them, I believe that all three had the impression that they were useless and perhaps burdens to their families.

This frame of mind in laboring men is most pitiable. Accustomed to daily physical work, they have an indescribable restlessness. One hears them say, "It seems as if I would go crazy without anything to do all day." I have heard this phrase used again and again by patients with injured shoulders, and often in the case of other injuries which cause only partial incapacity, but prevent getting jobs. Society should make some provision for these cases. There are few impaired men whose work is not worth a dollar a day, and many whose work is worth more, even when they take their own time in doing it. It is hard enough for able-bodied laboring men to get jobs and practically impossible for these convalescents, especially if they are elderly. Yet, as in the case of this carpenter, their experience itself has a value, and their advice alone is worth much to the ordinary man, who, for instance is trying to do a carpentering job. I think I could build a house myself if this carpenter sat by and told me what to do next, and how to do it!

As I have now retired from the active practice of general operative surgery I propose to devote my remaining professional life to this problem, especially so far as it concerns patients with lesions of the shoulder, in the diagnosis and treatment of which I am especially interested.

No patient will be too poor, if he will pay with what work he is able to do during or after his treatment. There are many patients attending charitable hospitals who could benefit from this plan. Industrial insurers might profit by the opportunity to send patients to be hardened up before they return to full time work, and some cases that are on relief might be rehabilitated. In certain penniless cases I might advance a payment of a dollar a day.

I own 90 acres of pasture and woodland just over the Hingham line in Norwell, Massachusetts. This land furnishes an abundance of light work, such as cutting out wild-cherry trees, burning brush and trimming dead branches, as well as heavier work, such as chopping, sawing and stacking wood from trees felled by the hurricane. It is obvious that under present economic conditions I could not hire labor at the usual rates to cut wild-cherry trees, saw off dead branches and so forth. The amount of increased value of the land would not justify the expense. On the other hand, if I could obtain

the labor for nothing undoubtedly I should eventually obtain a somewhat better price for the land. But I do not plan to get the labor for nothing—I exchange for it advice, which should have value from the many years I have devoted to the study of shoulder conditions and the time which it will take to examine these patients and to supervise their work. I do not plan to have this project a philanthropy but a fair exchange of labor. If I am successful, some such plan may be adopted by the State for individuals partially incapacitated by injuries other than those involving the shoulder. There is much idle unimproved land in this state, and many idle unimproved convalescents.

A co-operative spirit must be shown by the patients and in turn I shall study out ways in which they can use the rest of their muscles without abusing their shoulders, and set them at work that they can see will benefit me as well as themselves.

E. A. CODMAN M.D.

227 Beacon Street,  
Boston.

## REPORT OF MEETING

### HARVARD MEDICAL SOCIETY

A regular meeting of the Harvard Medical Society was held at the Peter Bent Brigham Hospital on March 12, with Dr. Soma Weiss presiding.

The first case presented was that of a forty five year-old man who four months before had had upper abdominal pain for one to two hours with no chills, fever, jaundice or nausea. An intravenous cholangiogram revealed "sand" in the gall bladder, and an operation was performed. This was a difficult procedure, a mass of induration at the ampulla was encountered and common-duct exploration was not carried out because of the patient's precarious condition. He was discharged improved, only to return after increasingly severe episodes of the same nature, except that they were accompanied by jaundice and vomiting. Laboratory data revealed a prothrombin time of 18 seconds, an icteric index of 33 and a blood cholesterol of 354 mg. per 100 cc. The findings were otherwise essentially normal. Ten milligrams of vitamin K were given preoperatively. At operation a similar mass of inflammatory tissue was found obstructing the ampulla and the abdomen was closed after the insertion of a catheter into the common bile duct. Dr. Elliott C. Cutler observed that the rapid loss of vitamin K during operations, even those of a minor nature, has not been well explained.

The second case was that of a forty nine year-old woman who developed successively headache, anorexia and jaundice about five months after the institution of arsenphenamine therapy for syphilis. Nausea and vomiting were experienced in the middle of the first course of arsenphenamine, thus Mapharsen was substituted, with relief of the vomiting. This in turn was replaced by Bismarsen in transmuscularly because of the persistent nausea; finally Bismarsen was superseded by bismuth subsalicylate when local soreness developed. On admission two days after the onset of jaundice, the icteric index was 60 and the prothrombin time and all other data were within normal limits. Treatment consisted of daily intravenous injections of 2 liters of glucose until oral feeding could be tolerated. The icterus remained at the initial level for about three weeks before starting to taper off while the prothrombin time remained normal throughout.

Dr. Weiss reminded the audience that acute hepatitis as a complication of antisyphilitic therapy is fast disappear-

ing. He stated that early reactions should be heeded as a warning of impending or subsequent liver damage, the symptoms of which may appear only after months. Recovery should be complete if proper supportive measures are carried out. Dr. Weiss emphasized how difficult it is to predict prolongation of the prothrombin time despite clinical evidence of severe liver damage.

The first speaker of the evening was Professor Louis F. Fieser of Harvard University who discussed "The Chemistry of Vitamin K." He recounted the work of Dam, Almquist and Doisy, who a year ago independently isolated the vitamin from alfalfa. The characteristic ultra violet absorption spectrum of the yellow oil was reported and Doisy described the probable chemical structure which he arrived at by careful degradation experiments. He concluded that the basic structure was a quinone radical with a long side chain. He computed that vitamin  $K_1$  should contain about twenty carbon atoms and vitamin  $K_2$  about thirty.

Dr. Fieser from a comparison of absorption spectrums, deduced that the fundamental compound was a naphthoquinone and probably had alkyl groups in the 2 and 3-positions. Knowing of several such naturally occurring compounds in which isoprenoid radicals were involved Dr. Fieser considered what combination of a naphthoquinone radical with these alcohols could give the necessary number of carbon atoms and double bonds. This line of reasoning gave the right answer for vitamin  $K_1$  and approached that for  $K_2$ , as it subsequently turned out.

By varying the technique of synthesis, Dr. Fieser was able within a few months to make 2-methyl-3-phenyl-1,4-naphthoquinone, which proved by bioassay and absorption spectrums to be identical with the vitamin  $K_1$  extracted from alfalfa. The compound was a clear yellow liquid completely insoluble in water and sensitive to light and alkali but otherwise chemically inert. A characteristic color reaction occurs when an alcoholic solution is treated with alkali, but this was not considered satisfactory as the basis of an assay method because the brilliant purple quickly fades to a dull red.

It was observed that related quinone compounds had a biological antihemorrhagic activity as assayed in deficient chicks. The most potent of these was 2-methyl-1,4-naphthoquinone, which proved to be three times as potent as the pure vitamin but also somewhat more toxic in very large doses. This compound is utilized in the synthesis of vitamin  $K_1$  in vitro and Dr. Fieser postulated that it may occur in vivo especially since its molecular weight is about one third and its activity about three times that of the complete vitamin according to chick assay.

Dr. Fieser described the extensive work on various naphthoquinone derivatives. In an attempt to correlate structure and function, activity was found to occur in those compounds having one long chain in either the 2 or 3-position and up to a certain point was roughly proportional to the length of this alkyl group. Long carbon chains in both positions rendered the compound inactive, and the addition of an ethyl rather than a methyl group in the 2 position reduced the biological activity a thousandfold. Alkylation of the non-quinonoid ring inactivated the compound. The cyclic oxide of 2-methyl-1,4-naphthoquinone and that of vitamin  $K_1$  itself were found almost as active as the parent product. This was considered significant because of the greater ease of keeping and handling these stable compounds. In an attempt to make a water-soluble substance, work on the esters of the hydroquinones was carried out and the so-

dium sulfuric ester of 2 methyl 1, 4 naphthohydroquinone was found on preliminary bioassay in chicks to be equivalent to vitamin K<sub>1</sub>

Observations on the clinical use of synthetic vitamin K<sub>1</sub> and associated compounds were reported by Dr Arnold M. Seligman, of the Beth Israel Hospital. As an introduction, he enumerated the factors involved in hypoprothrombinemia: the absence of the vitamin from the diet as seen in the newborn and in chicks, the absence of bile from the gastrointestinal tract, the lack of a normal intestinal mucosa for absorption, and severe liver damage. Clinical conditions corresponding to each of these groups were mentioned: hemorrhage disease of the newborn, obstructive jaundice or a biliary fistula, extensive intestinal resections or sidetrackings, ulcerative colitis, celiac disease and sprue, and any liver disease, such as cirrhosis. Factors which may increase the severity of an underlying deficiency include hemorrhage, the exudation of fibrin as in pneumonia, sepsis or repair, increased liver damage, the vomiting of bile and the combination of surgery and anesthesia.

Dr Seligman explained how the prothrombin time (Quick) is not notably affected until the blood prothrombin concentration reaches approximately 40 per cent of normal and does not increase markedly until the blood level reaches 25 to 15 per cent.

The synthetic vitamin was found to produce a satisfactory lowering of the prothrombin time when administered orally together with bile, but the effect of a single dose was not lasting. In the search for an intravenous method of using the water insoluble compound to obtain a longer duration and to obviate the necessity of giving bile, Dr Seligman found that a solution of 10 mg in absolute ethyl alcohol could be permanently suspended in non-particulate form in a liter of 10 per cent glucose solution. This solution was found under comparable situations and in minimal dosages to produce greater, more rapid, and more lasting decreases of prothrombin time than either the sodium sulfuric ester or 2 methyl 1, 4 naphthoquinone. When moderately large amounts were administered intravenously, all produced a fall of the prothrombin time within a few hours to normal limits, which persisted for varying periods.

Dr R. M. Kark reported that similar results had been obtained in obstructive jaundice at the Boston City Hospital by the intravenous route but that intramuscular injections produced effects which, although produced more slowly, lasted for five to six days. He also observed that attacks of cholangitis in such conditions prevent the effective utilization of the vitamin and that operations should not be performed during such periods of stress. Other instances of failure to affect the prothrombin time with vitamin K had been noted in cases of acute yellow atrophy, disseminated carcinomatosis and chronic liver disease.

## NOTICES

### AN ADDITIONAL STUDY TO EVALUATE ORIGINAL SEROLOGIC TESTS FOR SYPHILIS

More than five years ago the Committee on Evaluation of Serodiagnostic Tests for Syphilis, in co-operation with the United States Public Health Service, conducted a study to evaluate original serologic tests for syphilis or modifications thereof in the United States. The results of this study were published shortly after the investigation was completed (*J A M A* 104 2083-2087, 1935).

Consideration is now being given by the committee to the organization of a second evaluation study of original

serologic tests for syphilis or modifications thereof within the next year. If the need for an investigation of this kind seems to justify the cost, invitations will be extended to the authors of such serologic tests who reside in the United States or who may be able to participate by the designation of a serologist who will represent them in this country. The second evaluation study will be conducted utilizing methods comparable to those employed in the first (*J A M A* 103 1705-1707, 1934).

Serologists who have an original serologic test for syphilis or an original modification thereof and who desire to participate in the second evaluation study should submit their applications not later than October 1, 1940. The applications must be accompanied by a complete description of the technique of the author's serologic test or modification. All correspondence should be directed to the Surgeon General, United States Public Health Service, Washington, D. C.

## SOCIETY MEETINGS AND CONFERENCES

SEPTEMBER 2-6 — American Congress of Physical Therapy Page 852, issue of May 16

OCTOBER 6-11 — Annual meeting of Eye and Ear Specialists Page 81, issue of July 11

OCTOBER 8-11 — American Public Health Association Page 655 issue of April 11

OCTOBER 11, 12 — Pan American Congress of Ophthalmology Page 614, issue of May 23

OCTOBER 14-25 — 1940 Graduate Fortnight of the New York Academy of Medicine Page 938 issue of May 30

OCTOBER 21 — American Board of Internal Medicine Page 340 issue of February 29

JANUARY 4, 1941 — American Board of Obstetrics and Gynecology Page 1064 issue of June 20

APRIL 21-25, 1941 — American College of Physicians Page 1065 issue of June 20

## DISTRICT MEDICAL SOCIETY

### MIDDLESEX NORTH

JULY 31

OCTOBER 30

## BOOK REVIEW

*Jewish Contributions to Medicine in America From Colonial Times to the Present* By Solomon R. Kagan, M.D., foreword by Prof. James J. Walsh. Second edition—revised and enlarged. 8°, cloth, 792 pp., illustrated. Boston: Boston Medical Publishing Co., 1939. \$3.50.

The first edition of this book, published in 1934, covering the lives of Jewish physicians from 1656 to date, was reviewed in the June 20, 1935, issue of the *Journal*. At that time, it was pointed out, "We have reason to be extremely grateful to the author and the publisher and to all whose labors have made possible the compilation and publication of this admirable contribution to the history of medicine in America." Dr. Kagan has now re-published his volume and added about 250 pages, with a new index, bringing the subject up to date. It is an invaluable reference tool to librarians and in addition will be of interest to all physicians as a sound book for their library. The book, moreover, gives an excellent idea of the extensive and valuable contributions made by Jewish physicians to medicine in America. It is divided into sections: medicine, neurology and psychiatry, dermatology and syphilology, surgery, otolaryngology and ophthalmology; by gene and public health, and others. Thus, one can readily find a list of physicians who worked or are working in any special field. The book is well printed and published, and this revised and enlarged second edition is a distinct contribution to medical history.

# The New England Journal of Medicine

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VOLUME 223

JULY 25, 1940

NUMBER 4

## THE PHYSICAL GROWTH, THE DEGREE OF INTELLIGENCE AND THE PERSONALITY ADJUSTMENT OF A GROUP OF DIABETIC CHILDREN\*

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AND BYRON D. BOWEN, M.D. ||

BUFFALO, NEW YORK

THERE has been an interest for some time in the mental development of the diabetic child, as shown by the studies made by Joslin<sup>1</sup> and White,<sup>2</sup> who state that the diabetic child is superior mentally. West, Richey and Eyre,<sup>3</sup> in their study of intelligence levels of 76 diabetic children, state, "There are some mentally subnormal juvenile diabetics but the proportion of mentally superior is greater than among nondiabetics."

Brown<sup>4</sup> in a more recent study of diabetic children included data not only on the physical and on the mental development but also on personality traits. He states, "It was found that our group of diabetic children was distributed quite normally as to intelligence, 43 per cent of the diabetics are within the average I.Q. range, 90 to 100, with approximately equal numbers above and below." As to personality traits he says, "Increased irritability and excitability are the only significant personality changes noted by the parents, and no significant deviations are noted in the school or testing situation."

The present study was undertaken in order to collect as complete data as possible on an unselected group and to determine whether the diabetic child differs from the nondiabetic in physical growth, in intelligence, in school achievement and in personality adjustment.

### SUBJECTS

There were 49 children in this study—25 girls and 24 boys. During the course of the investigation 2 of the girls died, one from acute poliomyelitis

the cause of the death of the other could not be determined. The children had diabetes mellitus in various degrees of severity. They developed it before the age of fifteen years. Twenty-three became diabetic before the age of seven, 25 between the ages of seven and fourteen, and 1 after fourteen years of age.

The experimental group consisted of diabetic children attending the General and Children's hospitals in Buffalo, New York, and the private patients of one of us (B.D.B.).

The number of other children in the families varied from one to ten. Seventeen of the children were the oldest and 15 were the second child in the family. One child had a sibling who had diabetes; he had died before the discovery of insulin. There was one set of identical twins, one of whom was diabetic.

As to the hereditary factor, 2 of the children had a father who had diabetes. Eight of the children had a known paternal history of diabetes. 9 had such a history on the maternal side, in 2 both sides of the family were involved. Forty-five children were white and 4 were colored, 2 of the latter being partly Negro.

All but one of the children studied were American born. Both parents of 36 children were born in the United States, the parents of 5 of these children could trace their ancestry back to Yankee stock for several generations. The foreign elements consisted of German, Polish, English, Scotch, Irish, French, Czechoslovakian, Russian, Italian and Greek stock, but the German predominated. There were no Jewish children in the group. Thirty-nine children came from urban districts, and 10 from rural areas.

The parents of 14 of the children were able to pay for insulin and for medical care. Those of 25 bought insulin for their children but did not pay for medical care. Those of 10 could not pay for

\*A joint publication of the Buffalo General Hospital and Buffalo Children's Hospital. This study was promoted by Miss Ethel Schultz, her role in the problem itself is here dedicated.

†In Memory of Mrs. Grace Millard Knox.

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§Volunteer research fellow.

||Psychologist, Child Guidance Clinic, Buffalo Children's Hospital.

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either The complete educational record of both parents could be obtained in only 27 cases One parent of 5 of the children had not completed the eighth grade as compared with one parent of 22 of

TABLE 1 *Classification of Fathers of Diabetic Children*

GOODENOUGH GROUP	NO	PER CENT	PERCENTAGES OF EMPLOYED MEN IN THE UNITED STATES (GOODENOUGH)
I Professional	2	7	3.1
II Semi professional and managerial	6	20	5.2
III Clerical skilled trades and retail business	4	13	15.0
IV Farmers	2	7	15.3
V Semi skilled occupations minor clerical positions and minor business	8	26	30.6
VI Slightly skilled trades	5	17	11.3
VII Day laborers of all classes	3	10	19.5
Total	30		

them who had One of the parents of 22 of the group had either attended or graduated from high school One parent of 7 of the children had had a college education or its equivalent The fathers of 30 of the patients were classified according to the Goodenough<sup>5</sup> grouping (Table 1) As would

and laboratory findings, including height and weight measurements, were obtained for each child from the hospital record and at the time of individual interviews with the parents at home and at the hospital Both height and weight were observed on 20 girls and 18 boys, using the standards established by Engelbach<sup>6</sup> on the basis of chronological age More boys than girls fell below the minimum standard in height One of the boys had just recently developed diabetes, while the others had had the disease for four years or longer (Figs 1-4)

A number of psychological tests were given to each of the 49 children in the group These included the Revised Stanford-Binet Intelligence Scale,<sup>7</sup> the Ferguson Form Boards,<sup>8</sup> the Metropolitan Achievement Tests,<sup>9</sup> the reading, spelling and arithmetic sections of the New Stanford Achievement Test,<sup>10</sup> the Rogers Test of Personality Adjustment<sup>11</sup> and the Bernreuter Personality Inventory<sup>12</sup> In 5 cases where it was doubtful that an accurate measure of a child's abstract intelligence had been obtained, either the second form of the Stanford-Binet Scale, Form M,<sup>7</sup> or the Kuhlmann Anderson Scale<sup>13</sup> was added One child who was

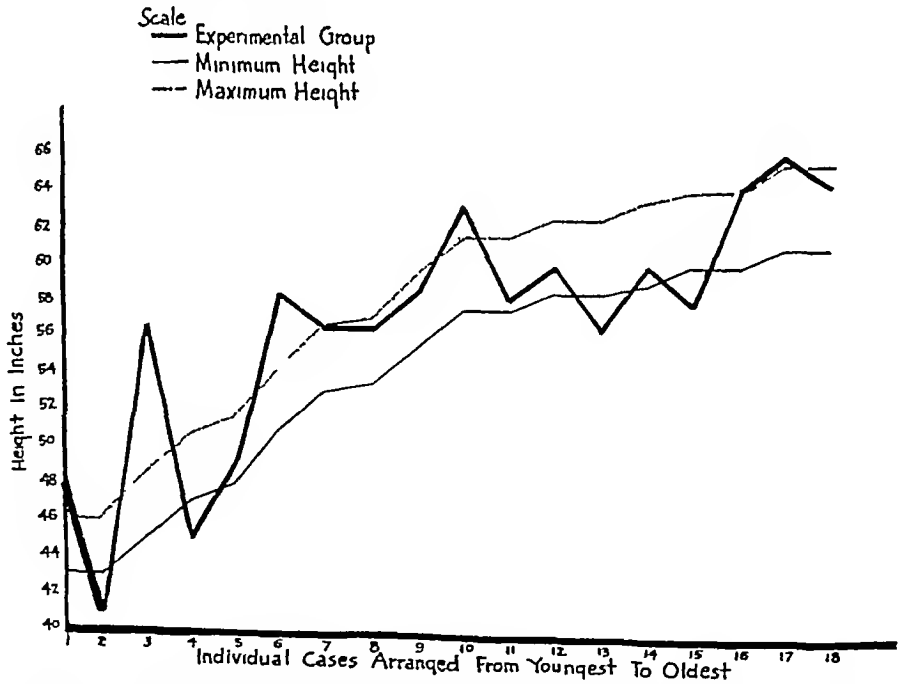


FIGURE 1 *Heights of Girls as Compared with the Minimum and Maximum Heights for Their Chronological Ages (Engelbach Norms) (Werner<sup>6</sup>)*

be expected, since more children came from urban communities, there were fewer farmers than would be present in the general population

EXPERIMENTAL PROCEDURE

The date of the onset of diabetes, the familial and developmental histories, the educational record

partially blind had the Hayes Revision of the Stanford-Binet Scale<sup>14</sup> In 5 cases the Ferguson Form Boards were not applied, because 2 of the children were too young, 1 was partially blind and 2 did not return to complete the tests Twenty nine children were given either the Metropolitan or the Stanford achievement tests, the choice of

test depending on the age. Thirteen children were beyond the ninth-grade level of the tests, 4 were at a preschool level, 1 was partially blind, 1 was

years of age, and the Bernreuter Inventory with those who were beyond this age level

Each child was interviewed by the psychiatrist,

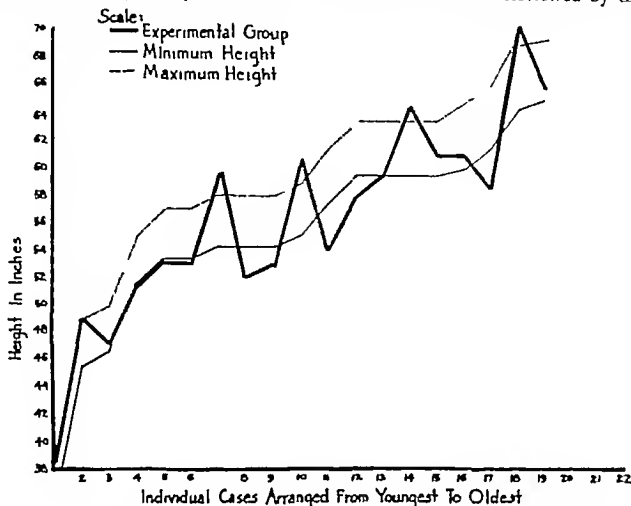


FIGURE 2. Heights of Boys as Compared with the Minimum and Maximum Heights for Their Chronological Ages (Engelbach Norms) (Werner's)

in a special class for retarded children and 1 had never attended school. Personality tests were included in the series, so that an objective measure

with the exception of 4, in order to determine his or her attitude toward diabetes, home, school, neighborhood, self and sex. In other words, an

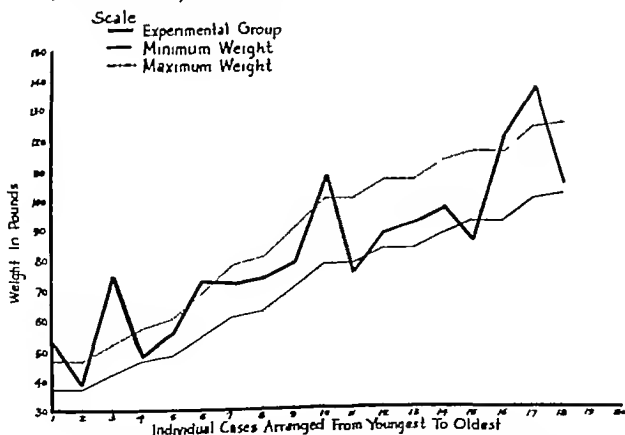


FIGURE 3. Weights of Girls as Compared with the Minimum and Maximum Weights for Their Chronological Ages (Engelbach Norms) (Werner's)

of the extent of the child's personality difficulties, in certain areas, could be obtained. The Rogers Test was used with the children from nine to thirteen

attempt was made to learn the child's mental attitude and trend of thought. One of the parents of each child was also interviewed to reinforce



the information gained and to learn the parents attitude toward the child and toward his or her physical condition

## RESULTS

### Physical Findings

Discounting the usual children's diseases and the diabetes, it was found that the experimental group as a whole was healthy. This was probably due to the fact that the children were under strict medical supervision. Only 6 children had prominent physical defects. Two had visual defects, one of these had defective vision which was

four months the boy's height had increased  $1\frac{3}{4}$  inches, making a total gain of  $2\frac{3}{4}$  inches in less than a year. The growth of the external genitalia and the development of pubic hair were very much faster when testosterone was used. The rapid development, however, might have been due entirely to the fact that the patient was taking a more adequate diet and was under strict medical supervision.

### Psychological Findings

Even though our experimental group is small, it is interesting that the distribution of the intelligence corresponds very closely to the intelli-

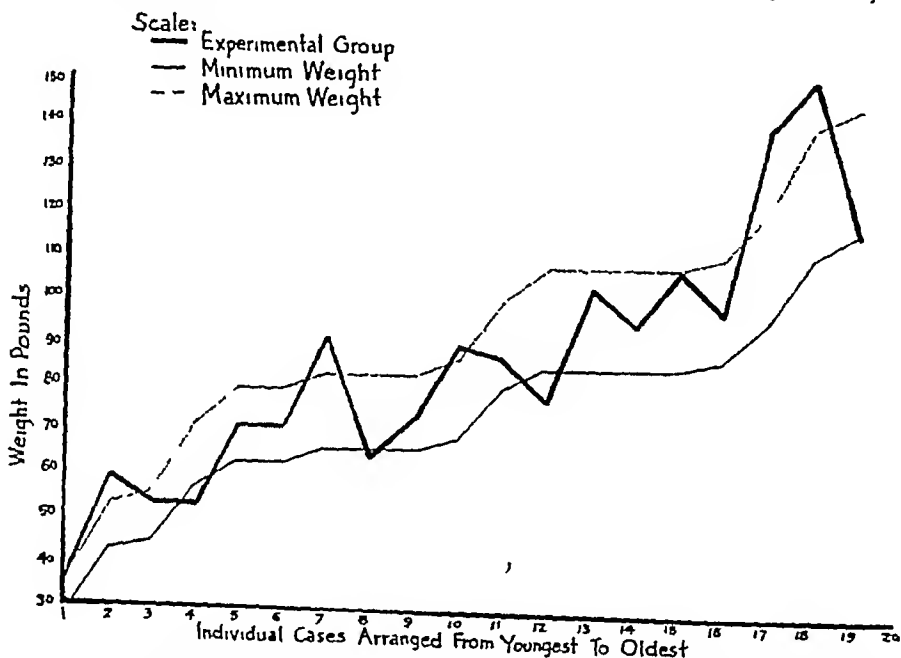


FIGURE 4 Weights of Boys as Compared with the Minimum and Maximum Weights for Their Chronological Ages (Engelbach Norms) (Werner<sup>6</sup>)

corrected by glasses, the other had bilateral cataracts. In the latter case, the cataract of the right eye was extracted in July, 1939, the other was to be done later. One boy had osteomyelitis with multiple foci, 1 girl, after a fracture of the right tibia in 1938, developed a bony cyst which was removed in June, 1939. One girl contracted syphilis and gonorrhea, and 1 boy had Vincent's angina. A sixteen-year-old boy who had had diabetes for eleven years, during most of which time he had not had consecutive medical attention, was below the minimum standard in both height and weight. He was given intramuscular injections of anterior-pituitary growth hormone every four or five days and 1 gr of thyroid daily. After six months of such therapy he had grown 1 inch and gained 10 pounds (Fig 5). This medication was then discontinued and intramuscular injections of 25 mg of testosterone propionate were administered every four to seven days. Within

the general population. Figure 6 gives a graphical picture of the distribution of the intelligence quotients on the Revised Stanford-Binet Scale,<sup>15</sup> as compared with that of the composite Forms M and L intelligence quotients for the children used by Terman and Merrill in standardizing this scale of tests.

The mean intelligence quotient of the experimental group was 103 and the standard deviation 16.8. In the standardization of the Stanford-Binet Scale the mean intelligence quotients ranged from 100 to 104, varying slightly for each age level, and the standard deviation was 16.4. So far as abstract intelligence is concerned, then, the children having diabetes used for the present study were not significantly brighter or duller than the large group of children on whom the standardization of the intelligence test was based. Possibly the impression that diabetic children are brighter comes from two sources. First,

quite a number of children who have had diabetes over a period of several years are short in stature. They may give the impression that they are brighter than one would expect children of their stature to be. Secondly, a great many of the children are able to inject their insulin and to take part in or be responsible for the weighing of

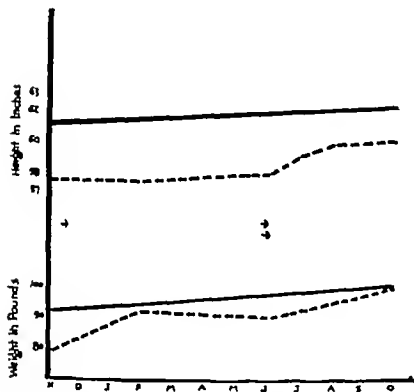


FIGURE 5. Growth Study During Treatment with Antuistrin G and Testosterone Propionate

The subject J G a sixteen year-old boy had been diabetic for about eleven years. The solid lines represent the standard minimum height and weight curves and the dotted ones those of the patient. The single arrow designates the beginning of the administration of Antuistrin G the double arrow that of testosterone propionate.

their food. On the surface this seems to be a complicated procedure requiring a good deal of intelligence, but if analyzed it is not found to be so.

The remaining tests included were of more value in understanding the patients educational problems and making recommendations for them as individuals.

The correlation between the mental ages of each child\* on the Revised Stanford-Binet Scale a measure of verbal intelligence, and those on the Ferguson Form Boards, a measure of form-space perception, was  $+ .62 \pm .06$ . Although not particularly high, this indicates a fairly marked tendency for the children with superior verbal intelligence to have superior form space perception, and vice versa. Only in a few scattered cases was there a marked difference between the two ratings (Fig 7†).

\*The exceptions were the children who were too young to be given the Ferguson Form Boards.

†PI of the group were not given the Ferguson Form Boards, so that they are not represented in the graph.

When educational achievement tests were given 1 of the group was found to have a severe reading disability and many were wrongly placed in school. One example was that of a girl who had been absent from school a great deal, giving as her excuse the fact that she had diabetes. She was twelve years of age at the time she was seen and was in the fourth grade, with children who were much smaller in size and much younger than she. On the basis of her ability and her achievement it was recommended that she be permitted to try sixth grade work. She was overjoyed at the prospect of being with children of her own age.

Of the 29 children who were given educational achievement tests, 9 appeared to be placed in a grade which was too difficult for them and 9 in too low a grade for their level of ability. The correlation between the mental ages of the children on the Revised Stanford-Binet Scale and their mean educational age on the achievement tests was  $+ .29 \pm .11$ . Figure 8 shows the individual differences.

It was interesting also to discover that on the basis of the mental age of the children on the

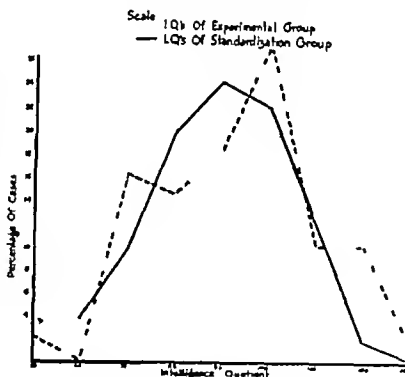


FIGURE 6. Polygon for Intelligence Quotient on Revised Stanford-Binet Scale (1937 Revision)

Revised Stanford-Binet Scale and their mean educational age on the achievement tests (admittedly not all inclusive criteria), 5 were working beyond the level of their ability in school and 10 were doing poorer work than one would expect of them. One example of this was the work of a pair of identical twins, only one of whom had diabetes but both of whom were examined. There was a strict father in the picture who expected great things of the boys. It was found that

both were working beyond the level of their ability in school, the one with diabetes being one year and seven months beyond the norm for his mental age level, and the one without diabetes being one year and five months beyond it.

A satisfactory personality test was not available for children under nine years of age, but with 2

of the group on which the test was standardized. However, the test has not been adequately standardized, so that too much value should not be placed on these findings.

The results for the Bernreuter Personality Inventory are given in Table 3. A high score for neurotic tendency on this scale indicates a tend

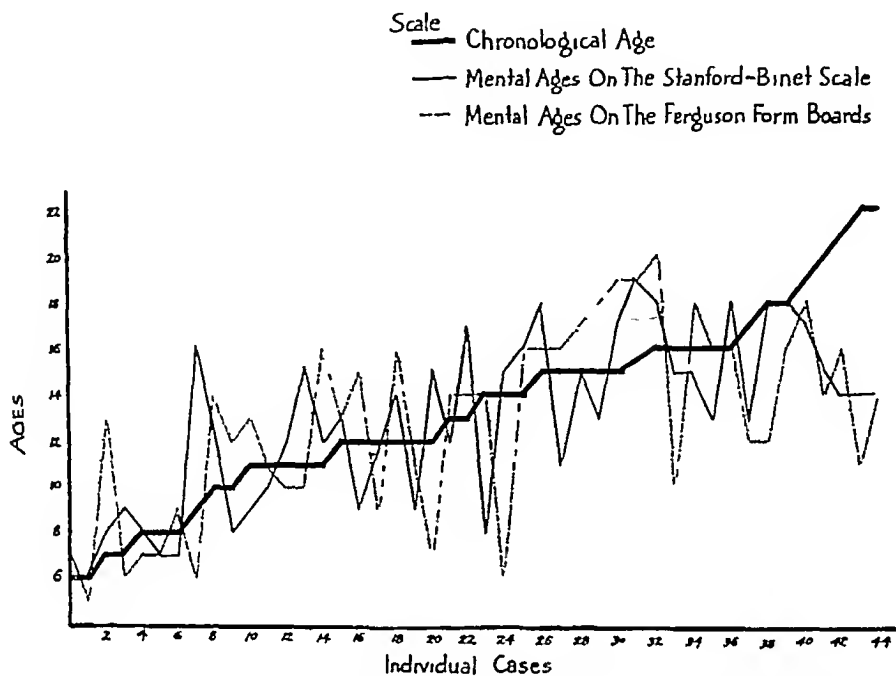


FIGURE 7 Chronological Ages and Mental Ages on the Stanford-Binet Scale and the Ferguson Form Boards

exceptions all the others were given either the Rogers Test of Personality Adjustment or the

TABLE 2 Results of the Rogers Test of Personality Adjustment in 18 Patients

PERSONALITY INFERIORITY			SOCIAL MALADJUSTMENT		
EXTENT	NO	PER CENT	EXTENT	NO	PER CENT
Low	9	50	Low	2	11
Average	5	28	Average	8	45
High	4	22	High	8	45
FAMILY MALADJUSTMENT			DAYDREAMING		
EXTENT	NO	PER CENT	EXTENT	NO	PER CENT
Low	5	23	Low	5	28
Average	8	45	Average	3	17
High	5	28	High	10	56

Bernreuter Personality Inventory, there being 18 in the group of nine to thirteen years of age to whom the former test was given, and 19 who were given the latter. The findings of the Rogers Test are listed in Table 2. Only 2 of the children did not rate high in any of these four areas, 7 rated high in one area, 6 in two, 3 in three and 0 in four.

There was some tendency for those of the experimental group to express more social maladjustment and to daydream more than did those

of the group on which the test was standardized. Three of the group were above the 75th percentile for this characteristic. Three were below the 25th percentile for the measure of self-sufficiency, showing a dislike for solitude and the frequent seeking of

TABLE 3 Results of the Bernreuter Personality Inventory in 19 Patients

MEASURE OF NEUROTIC TENDENCY			MEASURE OF INTROVERSION EXTROVERSION		
PERCENTILE NORMS	NO	PER CENT	PERCENTILE NORMS	NO	PER CENT
0-25	5	26	0-25	4	21
25-75	11	58	25-75	10	53
75-100	3	16	75-100	5	26
MEASURE OF SELF SUFFICIENCY			MEASURE OF DOMINANCE SUBMISSION		
PERCENTILE NORMS	NO	PER CENT	PERCENTILE NORMS	NO	PER CENT
0-25	7	37	0-25	4	21
25-75	8	42	25-75	9	47
75-100	4	21	75-100	6	32

advice and encouragement, while 5 were above the 75th percentile, indicating that they tended to prefer to be alone and to ignore the advice of others. Four tended to be more extroverted than introverted, while 5 were of just the opposite type. Four tended to be submissive, while 6

were inclined to dominate others in face-to-face situations.

### Psychiatric Findings

The psychiatrist found that the personality tests were valuable, as in some cases they provided data which might not otherwise have been uncovered and which were used in the psychiatric interview. In many cases the personality test gave the same analysis as that which was obtained by the psychiatrist. There were test results which were not "true," but they occurred only in the older mal

pressed themselves as having a feeling of shame because they had diabetes. Two of the 9 thought that other children avoided them because they had a "catching disease." One boy was so overwhelmed by the fact that he had diabetes that he was gradually withdrawing from social contacts and developing a shut in type of personality. These findings were borne out in his personality test. Another boy expressed feelings of guilt and interpreted diabetes as punishment. One girl stated that she felt her social prestige had been lowered with her associates when they

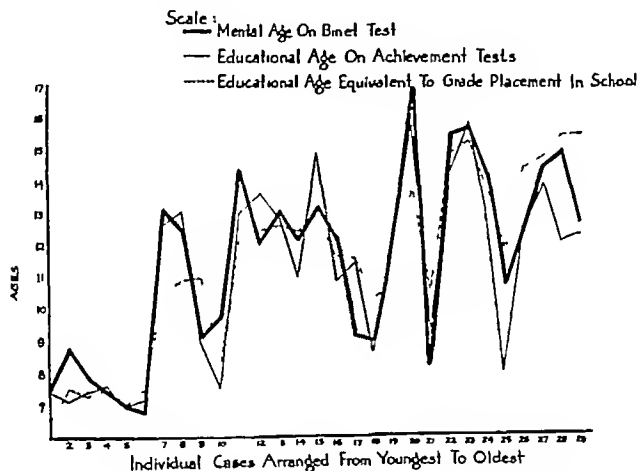


FIGURE 8 Intelligence as Compared with Grade Placement and Achievement

adjusted child, and the falsification of his answers was his method of protecting himself.

Of the 45 children interviewed, 13 seemed well adjusted. Eight of the 13 were below seven and a half years of age, and had developed diabetes before the age of four and a half years; the remaining 5 had had diabetes over several years but had developed it at a higher age level. The number of children presenting problems in the emotional field was 32. They expressed themselves as feeling "different from other children." This feeling created a conflict which expressed itself in various types of reaction: seclusiveness, aggressiveness, boastfulness and show-off behavior. There were several factors centering about the mental life of the child tending to cause this feeling of difference which created feelings of inferiority. They were as follows:

1. The diabetes itself often resulted in a feeling of difference. Nine of the children ex

learned that she had diabetes. There were 2 girls who resented their having diabetes because it placed them outside the "marriage market." One girl was so disturbed while discussing this that she became tearful. There were 2 boys who rebelled against diabetes. One believed that it was the cause of an osteomyelitis which kept him hospitalized for months at a time and interfered with his physical activities; the other refused to accept restrictions in diet, and frequently stole food, the ingestion of which was the cause of numerous attacks of acidosis.

It was interesting to find that the diabetes per se caused no emotional reaction in the very young child, except when the illness could be used as a means to gain an end by his threatening that illness would follow if he was not given his own way. Needless to say, the parent invariably gave in to avoid trouble. One child, aged seven, stated during the interview, "I

mustn't become emotional, as it is bad for me." Another interesting finding was that the earlier the child developed diabetes, the more readily he or she accepted it emotionally as part of the growing-up process, whereas those who developed it at a later age tended to rebel against it. Of the 28 children who had accepted the diabetes emotionally, 23 had developed it before the age of seven.

2 Underweight and understature made some children feel different (Figs 1-4). Of the 45 children interviewed, 24 were more disturbed emotionally over their short stature and loss of weight than by the fact that they had diabetes, 15 of the 24 reacted by becoming seclusive, and did not mix freely with their groups, 5 overcompensated for this by show-off behavior and boastfulness, exaggerating everything they said or did. One of these 5 children, a boy (Fig 5), was so disturbed by his short stature that he overcompensated by extreme boastfulness, not only of his physical prowess but also of his mental ability. Actually this was not borne out, as he failed to complete his first year in high school, although he was of average intelligence and was mentally able to achieve this. Since his stature and weight have been partially corrected, he seems less disturbed emotionally, and is more willing to co-operate about his diet, with the result that there has been a decided improvement in his diabetic state. Four children were attempting to solve the conflict of short stature and loss of weight: one boy by taking a physical training course, one boy by setting himself up as a chicken farmer, one girl by feeling secure with her new boy friend, saying, "He thinks I'm cute so I don't mind now being so short", one girl by reflecting the attitude, "Well, there is nothing I can do about it".

3 Other physical defects besides diabetes tended to make 3 children feel different from the group. One boy very much resented having osteomyelitis. Another boy was disturbed because of the fact he had a so-called "asthenic constitution," which interfered with his competitive life, as he became easily fatigued. One girl felt so inferior that she was unable to differentiate which disturbed her most, the diabetes, the short stature or the partial blindness.

4 Intellectual defects contributed to the inferiority of 5 children. They stated that no matter how hard they tried they never received good report cards, which caused criticism by the parents.

5 There were various social factors that entered into the production of conflict. In 1 case it was the problem of race. The child was part-

ly colored, and although of very superior intelligence, in fact having the highest degree of intelligence of the experimental group, she suffered from a marked sense of social inferiority. One boy felt inferior because he always fell short of the high standard set up by his father, who was a business executive. There were 7 girls and 2 boys who suffered severe conflicts in their attempt to emancipate themselves from the home. Unfortunately, the mothers were none too helpful in the crisis. One girl stated that she felt her mother loved her less since she had developed diabetes. Although the mother was not consciously aware of it, she was rejecting the child and was compensating for her feelings of guilt by constantly worrying about her, expressing her anxiety thus: "I never let her go anywhere because I think she will get knocked down by a car or she might have a 'spell,' and besides, her disposition has changed ever since she was told she had diabetes, and I just don't know what might happen to her." Both the parent and the child have been receiving intensive psychotherapy for the past few weeks, which has been helpful in lowering the tension in the home.

We found from the interviews with the parents that they did not differ from any other unselected group of parents. Several were unstable, and had personality difficulties of their own which they tended to project on to the child. Many of the mothers overprotected the child and were surprised when problems developed at a higher age level, while other mothers tried in every way possible to prevent the child from feeling different. Some were successful in their efforts, while others were not because they made too much of an issue of it. Three mothers stated that their children had "changed" since the onset of diabetes. One of these unconsciously rejected the child, which created the change, while the other two were unaware of the role their wrong handling of the child had played in contributing to it. Several mothers stated that their children were more irritable and harder to manage since the onset of diabetes. It was found in many cases that the irritability developed during periods of hypoglycemia, while in others it was found to be an outward protest against some disturbing element in the home. In 1 case it was the way the child had chosen to protest against an older sister who she felt was a rival. One mother expressed herself as being to blame for the child's diabetic condition, and had accepted willingly the "cross" she had to bear.

In a review of the psychiatric material, the emotional problems were found to be similar to those in other children. It is significant that

so few parents were not sufficiently aware of the child's emotional problems to seek advice.

#### SUMMARY AND CONCLUSIONS

Forty nine treated diabetic children in the City of Buffalo and western New York State have been studied from the standpoint of physical growth degree of intelligence and personality adjustment. The results were as follows:

**Physical** It was found that more boys than girls tended to be below the minimum height standard the weight of both sexes fell between the minimum and maximum standards. Only one child could be classified as a real dwarf, he was markedly improved by adequate injections of pituitary growth hormone and testosterone propionate.

Six of the 49 children had prominent physical defects.

**Psychological** The children were neither significantly brighter nor duller than non-diabetic children.

There was a positive correlation between verbal intelligence and form perception.

Several children were misplaced in school. A few were working beyond the levels of their ability.

There were some children who deviated from the normal in one or more personality traits, but not an excessive number for a small unselected group of children.

**Psychiatric** Thirty-two children were consid-

ered to be maladjusted. The diabetes itself was not the only contributing factor, physical and intellectual defects, as well as social problems, contributed to this maladjustment.

The earlier the child developed diabetes, the more readily he accepted it emotionally as a part of the growing up process.

It is important that parents receive advice in the handling of their children in order to prevent maladjustments from arising later.

#### REFERENCES

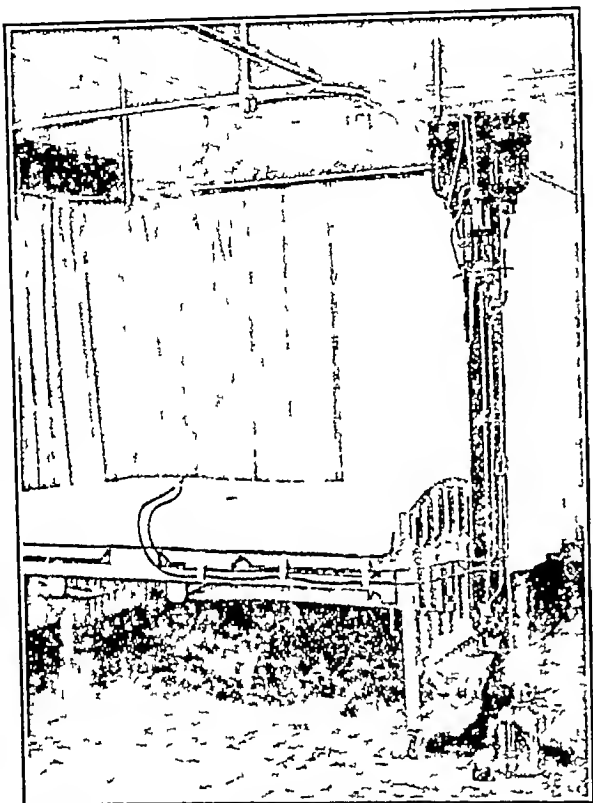
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## IRRIGATION AND TIDAL DRAINAGE\*

ARTHUR E. MACNEILL, MD† AND JOHN P. BOWLER, MD‡

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THE purpose of this paper is to describe certain modifications that we have made in previously described tidal-drainage apparatus, resulting in an instrument of wide urological application (Fig 1). The tidal-drainage apparatus of

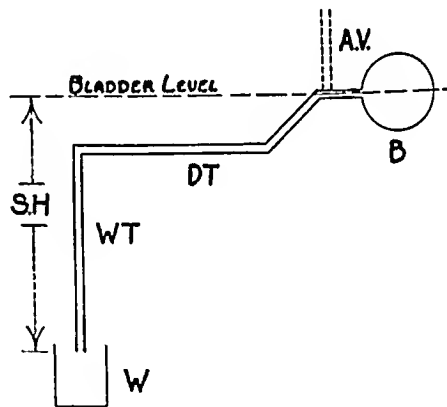
FIGURE 1 *Irrigation and Tidal Drainage Apparatus*

Munro and Hahn,<sup>1</sup> while suited to the care of abnormal bladders resulting from injury and disease of the spinal cord, has not been altogether satisfactory for the care of urological problems occurring independently of such damage. The apparatus here described accomplishes first, intermittent bladder drainage and filling, or tidal drainage, second, tidal drainage with succeeding irrigation, and third, automatic, interval bladder irrigation. There have been many contributions in this field, notably those of Laver,<sup>2</sup> Hinman,<sup>3</sup> Munro,<sup>1, 4, 5</sup> McKenna<sup>6</sup> and, recently, many others. That they have either been unappreciated or appear too for-

midable for general use is evident from the persistent use of conventional bladder drainage, consisting of an indwelling catheter, connecting tube and drainage bottle. We use the term "bladder drainage" to indicate closed drainage with a tolerated indwelling urethral catheter. Intermittent drainage and filling of the bladder involves a closed system within which it is desirable to have interval irrigation take place.

There are but few indications for bladder drainage which are not to be improved by irrigation and by functional exercise of the bladder. The conventional bedside drainage offers none of these possibilities, and when conducted with the ordinary technic provides many opportunities for infection. This is especially true when intermittent manual irrigation is added to the usual procedure.

With the apparatus as ordinarily connected (Fig 2), urine from the bladder (B) flows through the drainage tube (DT) and enters the

FIGURE 2 *Bedside Drainage*

waste bottle (W). If the tubing is sufficiently small to be filled by a column of urine, suction is developed on the bladder, the force varying with the distance between the lower end of the waste tube (WT) and the bladder. To prevent infection of the bladder, both the drainage tube and the waste bottle must be sterile. Otherwise, the respiratory motion of the urine in the tube will slowly transfer bacteria from the waste bottle to the bladder, either from the infected drop on the tube end, or from the waste fluid if the end of the tube is immersed. The weight of the column of urine in the waste tube exerts a constant suction, thus preventing normal filling and dis-

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Read at a meeting of the New England Branch of the American Urological Association, Boston, April 20, 1939.

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tention and promoting contraction of the bladder. The addition of an air vent (AV) will obviate this constant suction, as well as retard retrograde infection of the bladder, because the waste tube will be empty if air can enter it at the bladder level, and respiratory excursions will then occur only in the horizontal portion of the tube between the air vent and the catheter thus limiting ascending infection from the waste bottle.

The first step in the direction of a closed automatic apparatus is perhaps best taken by leading the catheter drainage into a closed bottle with an air vent (AV) (Fig 3). If ordinary bedside

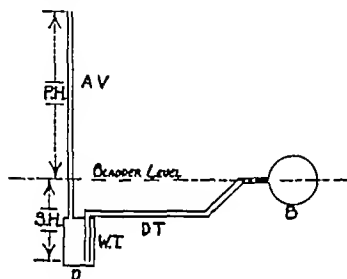


FIGURE 3 Portion of an Improved Bedside Drainage

drainage is changed so that urine flows into a drain bottle (D) only slightly below the bladder level, and air escapes from this bottle by way of the air vent, there will at first be a slight suction on the bladder, after the bottle fills and urine rises in the air vent, pressure will be exerted on the bladder. If this system were first filled with water and then connected to the bladder, it would constitute one of the many types of apparatus for decompressing the grossly distended bladder. As it stands, the apparatus would maintain pressure indefinitely and thus prevent bladder contraction so that intermittent emptying must be made possible.

This is easily accomplished by a simple syphon (S), the apex of which is set so as to start at the desired intravesical pressure as indicated by the level of fluid in the air vent tube, which has now become a cystometer (Fig 4). The urine will not flow from the top of the air vent, but instead will flow over the syphon as soon as the urine level in the air vent reaches the top of the syphon, and the bladder and the drain bottle will be evacuated. This suction or negative pressure can further be used for the activation of a second syphon for irrigating. The entire automatic nature of the final apparatus depends on the build

ing up of an intravesical pressure and its reduction by syphon action. A syphon works for the same reason that a leather belt will not stay on the back of a chair if one section is longer than the other: the longer section pulls over the shorter. The unbroken water column in a syphon acts in the same way: the weight of water in the longer arm pulls over the water in the shorter arm and this process continues indefinitely so long as liquid is supplied to the shorter side. When the fluid in the shorter arm is exhausted, air is drawn in and the flow interrupted.

The apparatus works as follows. Urine from the bladder flows into the drain bottle until it is filled. The pressure in the whole apparatus rises until the urine reaches the top of the syphon. It then flows down the long arm of the syphon into the waste bottle. The sucking action of the syphon is exerted on both the bladder and the

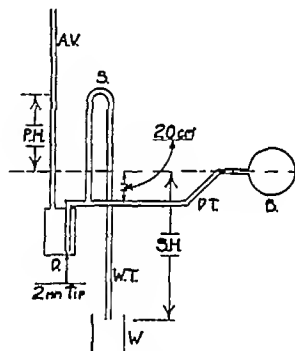


FIGURE 4 Improved Bedside Drainage

drain bottle, but the bladder empties first because it is higher, and also because the tube coming from the bladder is larger at all points than the 2 mm fused up of the tube descending into the drain bottle. When first the bladder and then the drain bottle are empty, air coming down the air vent is aspirated into the tip, runs up through the syphon and stops its sucking action. The cycle is repeated as often as the patient excretes enough urine to fill both the bladder and the drain bottle.

It will be seen that this apparatus imitates the normal filling and emptying of the bladder. Because it is easily kept sterile and because it distends the bladder and stretches mucosal folds, bladder infection should be prevented for a long interval. The apparatus should, we believe, be used in preference to ordinary bedside drainage



for the uninfected bladder requiring an indwelling catheter. It is obvious that the frequency of the drainage cycle is dependent on the urinary output of the patient, and therefore is slower than normal, because the drain bottle must be filled as well as the bladder. Hence, in order to maintain normal frequency an additional source of fluid must be added. This fluid is placed in the reservoir (R), is controlled by valve V, enters the system at X, and with the urine fills the drain bottle (Fig 5). When the pressure in the air

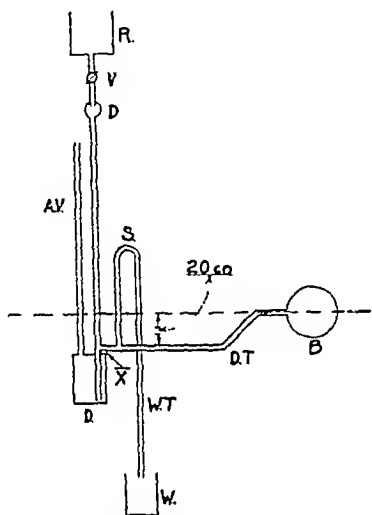


FIGURE 5 Tidal Drainage of Munro and Hahn

vent reaches bladder height, the urine in the drainage tube is displaced backward into the bladder, and the fluid enters the latter and mixes with the urine. The apparatus fills up and empties as before, but the use of additional fluid ensures that it will drain and irrigate at regulated intervals. The irrigating effect of this fluid is dependent on the size of the bladder, and a bladder whose capacity is less than the volume of urine displaced backward from the drainage tube will not be irrigated. The apparatus shown in Fig 5 is the tidal-drainage apparatus described in 1935 by Munro and Hahn<sup>1</sup> and used by them for the care of abnormal and infected bladders secondary to injuries and diseases of the spinal cord.

We have made a change in the apparatus which guarantees irrigation regardless of the size of the bladder being treated. The irrigating fluid, instead of entering the system at X, turns the corner and flows through its own tube, as the arrow indicates, toward the bladder (Fig 6). It enters the system through one arm of a Y tube at the catheter. Thus, when the pressure in the apparatus rises higher than the bladder level the bladder immediately starts filling with irrigating fluid, because only the urine in the catheter needs to be displaced back

into the bladder before irrigating fluid can enter. The urine from the bladder flows into the drain bottle (D) by its own tube (DT) and always in one direction, except for slight respiratory oscillations. This is an additional protection against retrograde infection. We believe that the Munro apparatus should be modified in this manner.

The irrigation obtained with this modified apparatus is not satisfactory for the care of grossly infected bladders, because there is always a mixture of irrigating fluid and urine in the bladder, and it is never irrigated rapidly. We have therefore made another addition to the apparatus to obtain one or more irrigations of the bladder after each tidal drainage cycle (Fig 7). Possibly the complicated appearance of this diagram will delay the use of such apparatus, but there is only the addition of a second system of reservoir and syphon activated by the suction created in the tidal-drainage cycle.

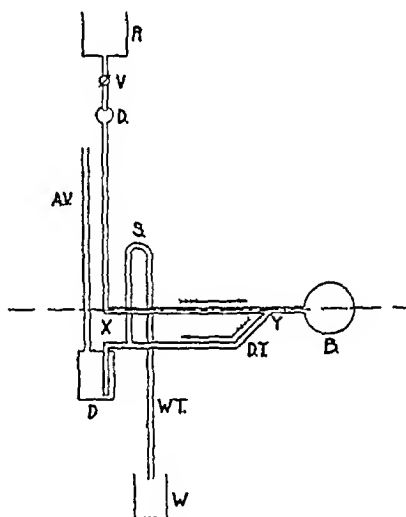


FIGURE 6 Improved Tidal Drainage

When the bladder is being aspirated in the course of the operation of the tidal-drainage apparatus, suction is exerted through the irrigation tube (IT), which draws water from an irrigation bottle (IB) over the top of a syphon (S<sub>2</sub>). The water from the syphon drops through a dropper (D<sub>2</sub>) at a rate controlled by valve V<sub>2</sub>, but the rate is slow enough so that the tidal-drainage apparatus still empties the bladder and the drain bottle. When syphon S<sub>1</sub> stops operating, however, syphon S<sub>2</sub> continues to supply clear irrigating fluid to the system, this rapidly fills the drain bottle and the bladder. The pressure is raised until syphon S<sub>1</sub> again empties the system. The remaining fluid in the irrigation bottle then runs through the system and drains into the drain bottle, at which point air enters the lower end of syphon S<sub>2</sub> and its action is stopped. By increasing the amount of

fluid in the irrigation bottle the bladder can be irrigated two, three or more times following each tidal-drainage cycle.

As the pressure in the apparatus increases during the irrigation cycle, air displaced back up the irrigation tube increases the back pressure, slows the rate of dropper  $D_2$  and delays the last part of the cycle. This is undesirable, because the maximum pressure might then be maintained on the bladder for several minutes, or until dropper  $D_1$  supplies enough fluid to start syphon  $S_1$ . Instead of a flap valve below dropper  $D_2$  which would allow the air to escape and thus avoid this possibility, we have attached an expansion chamber ( $EC$ ), made of Penrose tubing,  $1\frac{1}{4}$  inches wide and 6 inches long, sealed at one end and attached to the irrigation tube at the other. Penrose tubing is ordinarily flat, but increased air pressure in the irrigation tube dilates it very easily, and back pressure on the drainage tube is thereby avoided. At the end of the irrigating cycle, the descending column of fluid in the irrigation tube aspirates the air from the Penrose tubing and makes the latter ready for the next cycle. Since infection entering through a flap valve would be more dangerous on the irrigating side of the apparatus and because most flap valves will not stand sterilization we believe that the closed expansion chamber is

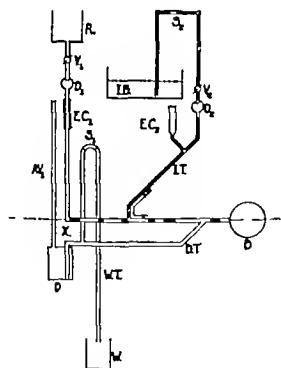


FIGURE 7 Step in Adding Irrigation to Tidal Drainage

a better solution of this difficulty. A similar device should be placed below dropper  $D_1$  if syphon  $S_1$  is higher than 12 inches above the pubic level, but here the substitution of 6 inches of  $1\frac{1}{4}$ -inch Penrose tubing for the same length of regular tubing below dropper  $D_1$  will suffice.

The adjustment of the height of syphon  $S_1$  has not been satisfactory in some of the tidal

drainage models, because the rubber tube eventually flattens out at the peak of the syphon if it is hung over a bar or similar device. By taking an ordinary keyhole-shaped curtain ring, covering it with a rubber tube and attaching the syphon, a smooth loop is obtained without constriction of the tube at any point, with the added advantage that the syphon can be raised or lowered by as little as a millimeter at a time, and through a very wide range.

The next and slightly more complicated diagram (Fig 8) illustrates the method of filling the ir

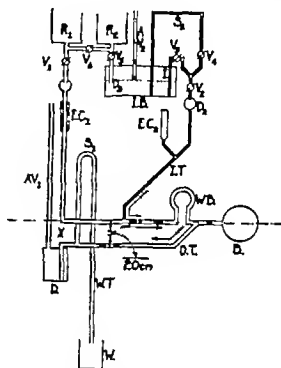


FIGURE 8 Tidal Drainage and Irrigation with Added Interval Irrigation

rigation bottle ( $IB$ ). An additional reservoir ( $R_2$ ) supplies fluid for dropper  $D_2$ , which is controlled by valve  $V_2$ . This fluid drips into the irrigation bottle at a slower rate than dropper  $D_2$  runs, yet fast enough to fill it at regular intervals when syphon  $S_2$  has run dry. The irrigation bottle can continue to fill only until the irrigating fluid reaches the lower end of air vent  $AV_2$ . Air can then no longer escape from the chamber and the irrigating fluid rises up the syphon arm ( $S.$ ) and up air vent  $AV_2$  until these levels are the same as the level of the irrigating fluid in reservoir  $R_2$ . Dropper  $D_2$  then stops running because the pressures on both sides of it are equalized. Syphon  $S_1$  is then ready to be started by the aspirating action of syphon  $S_1$  at the next tidal-drainage cycle.

If syphon  $S_2$  is thrown out of operation by closing valve  $V_1$ , and tube  $I$  is opened by turning valve  $V_2$ , an automatic irrigator is made that runs independently of the tidal-drainage cycle. After the pressure rises in  $AV$  water will flow over the top of tube  $I$  because it is at all times at a level lower than the fluid in reservoir  $R$ . This starts an

irrigation through the irrigation tube without any aspirating action from the tidal-drainage portion of the apparatus. In this way, by the simple clamping and unclamping of a valve, the apparatus can be made to work as an interval irrigator. Valve  $V_6$  may be used to disconnect reservoirs  $R_1$  and  $R_2$ , if it is desired to irrigate with a different fluid from that used in the tidal-drainage apparatus.

In patients having bladder sensation, the use of irrigation with water even as cold as room temperature is uncomfortable, often enough so to awaken the patient at night. For this reason, as well as for the therapeutic advantages, we have used a thermostatically controlled water bath to heat the irrigating fluid just before it reaches the patient. This is done by leading the fluid through a circular glass tube ( $WB$ ) immersed in water at approximately  $100^{\circ}\text{F}$ . The irrigation is slow enough to ensure adequate heat transference with about 18 inches of 5 mm glass tubing immersed in the water. A very simple water bath, heated by a 40 watt electric-light bulb, has proved satisfactory.

The advantages of this apparatus are as follows:

The positive pressure on the patient's bladder is at all times controlled by the height of syphon  $S_1$ .

The irrigation following each tidal-drainage cycle dilutes both the contents of the drain bottle and of the bladder, and thus ensures complete cleaning of the apparatus at each cycle.

Because of the large volume of irrigating fluid used, antiseptics should not ordinarily be necessary; we have had very good results in a variety of bladder infections with boiled water alone.

No method of hand irrigation can equal this apparatus in economy of time, protection from overdistention and avoidance of the infection incident to disconnecting the catheter while irrigating with a bulb syringe.

Nursing care is simplified, because the only requirements are adequate amounts of irrigating fluid for reservoirs  $R_1$  and  $R_2$  and the removal of waste as it accumulates in the waste bottle.

Because of the copious irrigation, the apparatus will remain sterile for long periods of time; we see no reason for sterilizing it as often as is necessary with the tidal-drainage apparatus.

No special glass-blowing is required. The apparatus can be made from parts available in any hospital supply room.

The apparatus operates on hydraulic principles, and there are no moving parts or exposed metal parts to corrode; the energy that operates the device is supplied by the lifting of fluid when it is being poured into the reservoirs.

#### SUMMARY

An improved method of bedside bladder drainage has been devised. The Munro-Hahn tidal drainage apparatus is reviewed and modifications recommended. A device is described which when connected to the improved tidal-drainage apparatus may be used either to irrigate the bladder after each tidal-drainage cycle, or independently as an interval irrigator.

The construction details of the apparatus, together with a list of the necessary materials, will be included in the reprints of this paper.

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## NEW HAMPSHIRE MEDICAL SOCIETY

## PROCEEDINGS OF THE

## ONE HUNDRED AND FORTY NINTH ANNIVERSARY

House of Delegates, May 13, 14 and 15, 1940

THE House of Delegates convened at the Hotel Carpenter, Manchester, on Monday evening May 13, 1940, at 7.30, with Speaker Fred Fernald, of Nottingham, presiding

The following members answered the roll call

The President, *ex-officio*  
 The Vice President, *ex-officio*  
 The Secretary Treasurer *ex-officio*  
 Chester L. Smart, Laconia  
 Earl J. Gage, Laconia  
 Francis J. C. Dube, Center Ossipee  
 W. J. Paul Dye, Wolfeboro  
 Norris H. Robertson, Keene  
 Leander P. Beaudoin, Berlin  
 Lewis C. Aldrich, Jefferson  
 Leslie K. Sycamore, Hanover  
 John C. Eckels, Lisbon  
 Frederic P. Lord, Hannover  
 Deering G. Smith, Nashua  
 Henry O. Smith, Nashua  
 Clarence E. Dunbar, Manchester  
 George V. Fiske, Manchester  
 Luther A. March, Nashua  
 Clarence E. Butterfield, Concord  
 Warren H. Butterfield, Concord  
 Charles H. Parsons, Concord  
 Fred Fernald, Nottingham  
 Frederick S. Gray, Portsmouth  
 James Sanders, Rye  
 Edna Walck, Dover  
 Henry C. Sanders, Jr., Claremont  
 Addison Roe, Newport

SPEAKER FERNALD I declare a quorum present I appoint the following for the Credentials Committee Earl J. Gage, Warren H. Butterfield and Clarence E. Dunbar

I appoint the following for the Committee on Officers Reports Norris H. Robertson (chairman), Deering G. Smith and Frederick S. Gray

I appoint the following for the Committee on Memorials and Communications Chester L. Smart, George V. Fiske and James Sanders

Is the Committee on Credentials ready to report?

DR. CLARENCE E. DUNBAR We find the credentials are all in order

SPEAKER FERNALD The minutes of the last meeting are published in the 1939 transactions of the New Hampshire Medical Society What is your pleasure about the reading of these minutes?

DR. FRANCIS J. C. DUBE I move that the reading of the minutes be omitted

This motion was seconded and was carried

SPEAKER FERNALD Our next order of business will be the report of the Secretary Treasurer

*Report of the Secretary-Treasurer*

The following report for the year 1939 is submitted

## MEMBERSHIP DECEMBER 31 1939

	PAID	
Belknap County	30	
Carroll County	15	
Cheshire County	29	
Coos County	40	
Grafton County	65	
Hillsborough County	127	
Merrimack County	75	
Rockingham County	54	
Strafford County	29	
Sullivan County	19	
Not in county society	6	
	489	
	UNPAID	
Affiliate Members	26	
Honorary Members	11	
	37	
Total	526	

The total membership on December 31 1938 was 531

## FINANCIAL STATEMENT

	RECEIPTS	
January 1 1939—balance forward	\$1,063.47	
Net receipts 1939 annual meeting	83.38	
Belknap County	192.00	
Carroll County	96.00	
Cheshire County	186.00	
Coos County	222.00	
Grafton County	384.00	
Hillsborough County	786.00	
Merrimack County	444.00	
Rockingham County	306.00	
Strafford County	174.00	
Sullivan County	114.00	
Refund, Cancer Commission	17.93	
Members not in county societies	36.00	
Benevolence Fund (Women's Auxiliary)	50.00	
Cash received at annual meeting	49.00	
Subscription (New England Journal of Medicine)	3.00	
	\$4,206.78	

EXPENDITURES

<i>New England Journal of Medicine</i> (tabulation)	\$17 74
<i>New England Journal of Medicine</i> (transactions)	534 94
<i>New England Journal of Medicine</i> (journals)	567 52
<i>New England Journal of Medicine</i> (full subscription, one member)	3 00
Carleton R Metcalf	400 00
Bridge and Byron (printing)	67 25
Envelopes, stamps and postcards	128 67
Eagle and Phoenix Hotel Co (committee lunches)	21 05
Robert O Blood, treasurer (telegrams and telephone calls)	22 51
Western Union (telegrams to Washington)	9 18
Women's Auxiliary	100 00
Benevolence Fund	553 00
Frank J Sulloway (retaining fee)	100 00
George C Wilkins (Cancer Committee)	50 00
Warren H Butterfield (refund on one member)	6 00
Concord Photoengraving (half tone cuts)	27 42
The Barwood Press (Commonwealth Fund)	19 71
Dartmouth College (Committee on Medical Education and Hospitals)	9 75
Deering G Smith (expenses, A M A meeting)	143 36
Eric M Matsner (expenses, annual meeting)	25 00
Louis A Buie (expenses, annual meeting)	98 00
W Wayne Babcock (expenses, annual meeting)	27 70
Charles W Tobey (expenses, annual meeting)	44 25
Madeline A May (stenographer, annual meeting)	247 13
Deering G Smith (dues collected at annual meeting)	35 00
Warren H Butterfield (dues collected at annual meeting)	7 00
Wendell P Clare (dues collected at annual meeting)	7 00
	<hr/>
Balance, January 1, 1940, in checkbook	\$3,272 18
	1,210 84
	<hr/>
	\$4,483 02
Net receipts, 1938 annual meeting, deposited 2/21/39	246 24
Dues for 1938, deposited 1/20/39	30 00
	<hr/>
	\$4,206 78

The Society is in good financial condition with all debts paid and a balance of \$1210 84 in the bank on December 31, 1939

The Benevolence Fund on the same date amounted to \$2347 06 Of this amount the principal is \$2117 19 and the accrued income \$229 87 During the past year we have received from the Women's Auxiliary \$50 for this fund Since January 1, 1940, we have allotted \$1000 to the Permanent Fund held by the Trustees

One of the officers of the Society died during the past year Alpha H Harriman, of Laconia, a trustee emeritus

The President has the privilege of appointing two officers Dr Woodman chose for the Anniversary Chairman, Ezra A Jones, of Manchester, and for the member of the New England Medical Council, David W Parker, of Manchester

A year ago the House of Delegates made the following recommendations, which have been carried out

1 A group of five ophthalmologists has advised the State Department of Public Welfare concerning the care and treatment of the blind

2 The Committee on Amendments to the Constitution and By-laws was asked to compare our constitution and by laws with those of the American Medical Association

3 Fifty dollars was sent to the Committee on the Control of Cancer for the furtherance of its work. Another \$50 was left with the Committee on Child Health for use in the distributing of its literature.

4 The State Board of Health was queried about the possibility of providing hospitalization and fever treatment for neurosyphilitic patients The Board reported that it had received a grant-in-aid of \$2000 for this purpose from the United States Public Health Service.

5 Members of Congress were advised that the Society is opposed to the Wagner Bill

6 The general hospitals in New Hampshire were notified that the House of Delegates approved routine blood examinations for syphilis on all patients

A report has recently been issued on the results of the premarital tests for syphilis The statute provides for a blood test with a statement by the physician that the applicant is not infected with syphilis or in a state which may become communicable A positive blood test in itself does not prevent marriage.

During the first twelve months of enforcement there were 10,363 applicants Eighty-one applicants gave positive tests, 47 of these were residents of New Hampshire.

The report shows a decrease in marriages 5065 in 1939, as compared with an average of 7289 during the years 1933-1937 The entire decrease, however, was due to the fact that fewer residents of Massachusetts came to New Hampshire to be married

On October 1, 1939, every physician who had been sent a positive report was asked

- (a) Was the patient allowed to be married?
- (b) Was he [the physician] treating the patient?
- (c) If not, did he know what had become of the patient?

This information was obtained on 70 of the applicants. Forty nine had been allowed to marry Of the 21 not allowed to marry, 11 were women Four of the 11 women were forty-five years of age or over, that is, beyond the usual child bearing period None of the applicants who were denied marriage had been aware of their infection Seven of the 21 who were denied marriage had been placed under treatment in consequence of the premarital blood test.

Of the 49 applicants who were allowed to marry, 4 were under active treatment before applying for the premarital certificate. Of the 45 not previously under treatment, 8 were placed under treatment because of the test.

The premarital law protects the future child by notifying the woman and her physician of the infection If a mother has adequate treatment during pregnancy the child will be healthy

It is obvious that during the first year there was not an adequate check up on positive cases, but since October 1, 1939,—the first anniversary,—the State Board of Health has kept a close check on these cases so that practically every positive case is now getting treatment.

The law has been effective in discovering syphilis in persons unaware of infection, and it has had an excellent educational effect on the public and on the physicians. The physicians should see to it that all these positive cases are treated

A suggestion has been made that our meetings revert to their former type by having papers read during the

mornings by members of the Society in place of the present round-table discussions. I believe that it is difficult to get a member of the Society to write a paper and still more difficult to get him to write a good paper. Further more, I think that our members get more out of round table conferences than they do out of set papers. How ever I bring the matter to your attention because I have been asked to do so.

Governor Murphy asked us to name two members of the Society to serve on the Committee on Infantile Paralysis. Dr Woodman appointed Carl R. Friberg of Manchester and Ralph W. Hunter of Hanover. These appointments should be confirmed by the House of Delegates.

We were also asked to appoint someone to serve on the committee that is revising the *Pharmacopoeia*. Dr Clarence J. Campbell of Dartmouth College who is at tending this convention offered to represent us as well as his college. Dr Campbell's appointment should also be confirmed by the House of Delegates.

CARLETON R. METCALF Secretary

DR. NORRIS H. ROBERTSON The Committee on Officers' Reports would emphasize that the pre marital test is for the purpose of finding new cases, not of preventing marriage, and of treat ing these new cases and thereby preventing con genital syphilis.

We recommend that the medical certificate be confined to the requirements of the State law.

I move the adoption of this portion of our re port.

This motion was seconded and was carried.

DR. ROBERTSON The committee recommends the continuation of the round-table discussions.

I move the adoption of this portion of our report.

This motion was seconded and was carried.

DR. ROBERTSON The committee recommends the confirmation of the appointments of Carl R. Friberg of Manchester, and Ralph W. Hunter of Hanover, to serve on the Committee on Infantile Paralysis.

I move the adoption of this portion of our re port.

This motion was seconded and was carried.

DR. ROBERTSON The committee recommends the confirmation of the appointment of Clarence J. Campbell, of Dartmouth College, to represent the Society on the Committee for the Revision of the *Pharmacopoeia*.

I move the adoption of this portion of our report.

This motion was seconded and was carried.

DR. ROBERTSON The committee recommends the confirmation of the appointment of Andrew

L. MacMillan, Jr., of Concord, to the Medical Advisory Committee of Eye Conditions.

I move the adoption of this portion of our re port.

This motion was seconded and was carried.

SPEAKER FERNALD We will now hear the re ports of the councilors.

### *Belknap County*

The Belknap County Medical Society held six monthly meetings this past year from November to April inclu sive, with a very good attendance.

Two outstanding speakers at the meetings were Dr. Frazer B. Gurd of Montreal and Dr. Cadis Phipps of Boston.

The president, Dr. J. B. Woodman and the secretary Dr. C. R. Metcalf of the New Hampshire Medical So ciety were guests at one of the meetings.

The society has gained three new members and has lost one member by death.

CLIFTON S. ABBOTT

### *Carroll County*

The Carroll County Medical Society had two meetings scheduled for the year. Due to unavoidable conditions however the usual fall meeting was omitted. We are now looking forward to our spring meeting which will be held shortly before that of the New Hampshire Medi cal Society.

While our group is small in number our membership is nearly 100 per cent, and we believe that our gather ings are successful.

CHARLES E. SMITH

### *Cheshire County*

The Cheshire County Medical Society held two meetings during the past year, one social and one business meeting.

The annual meeting was held in the Doctors' Library, Elliott Community Hospital, December 4, 1939. At this meeting the officers for the coming year were elected, routine business was taken up, and three new members were admitted. This was one of the best attended meet ings that Cheshire County has had in several years. In teresting papers were read by visiting and local men fol lowed by lengthy discussions.

At the conclusion of the meeting, luncheon was served under the supervision of the hospital dietitian.

JOHN J. BROWNAN

### *Coos County*

The Coos County Medical Society is in good condition. We have two meetings a year and they are always well attended with much interest shown by the members.

A committee from this society is assisting the County Fiscal Agent in his efforts to keep medical relief within reasonable bounds.

Our membership is gradually increasing.

RICHARD E. WILDER.

### *Grafton County*

The thirty sixth annual meeting of the Grafton County Medical Society was held October 12, 1939 at the Mary Hitchcock Memorial Hospital.

Dr Putnam, in behalf of the censors, presented the names of Radford C Tanzer, Arthur E MacNeill and John S Lyle, all of Hanover, and these applicants were duly voted into membership.

The Committee on the Farm Security Insurance Program reported that it had met with similar committees from Sullivan and Cheshire counties, and that a fee schedule had been drawn up for use in cases treated under this program. The schedule was presented to the society and received without dissent. Recommendations from the Committee on Medical Economics of the New Hampshire Medical Society relative to the program were read and discussed. It was pointed out that it would be advisable in any statement sent out concerning the plan to state definitely what services were not included in the plan (such as laboratory and x-ray examinations) as well as the procedure for handling these extras. The committee was instructed to continue its study in co-operation with the committees from the other two counties and to report back to the society before final action should be taken.

President McKinlay appointed the following committees:

Nominating W F Putnam, H C Pickwick, H L Johnson

Public Health and Legislation E. M. Miller, H N Kingsford, J G Bogle.

Advisory to Women's Auxiliary the president, H T French, W F Putnam

Auditors R E. Miller, C C Stewart

The Nominating Committee brought in the following nominations, which were duly confirmed:

President J C Eckels

Vice president S M Gundersen

Secretary treasurer L. K. Sycamore.

Censor B Beattie.

Member of Committee on Medical Jurisprudence J F Gile.

Delegate L. K. Sycamore.

The scientific program consisted of a highly informative discussion by Dr Chester M Jones, of Boston, on "Medical Aspects of Gall Bladder Disease."

Following the meeting, luncheon was served in the hospital dining room.

On December 18, 1939, a special meeting was convened to give final approval to the program of general practitioner care for clients of the Farm Security Administration. L K Sycamore, for the committee, reported that the program was ready to be put into effect January 1, 1940, in Cheshire and Grafton counties, and that Sullivan County had withdrawn from the plan. The regulations drawn up by the intersociety committee were discussed, and a few minor changes suggested. It was then moved and seconded that 'the society approve the program for initiation of the plan in Grafton County as of January 1, 1940.' It was voted that L. K. Sycamore be named auditor for the Farm Security medical program in Grafton County, and that the president appoint two other members to a Reference Committee. A W Burnham and E. M. Miller were later appointed in this capacity by the president.

The regular spring meeting of the Society was held at the New Hampshire Sanatorium, Glencliff, on Thursday, April 18, 1940. The business meeting was followed by a scientific session, which consisted of a 'Symposium on Tuberculosis,' conducted by Drs R. M. Deming, Frank Seligson and M D Tyson. Luncheon was served.

A. W. BURNHAM

## Hillsborough County

The Hillsborough County Medical Society held two very interesting meetings.

The annual meeting of the Hillsborough County Medical Society was held at Milford on November 14, 1939, at which four new members were admitted and four applicants were rejected. The refugee-physician problem provoked a very free discussion. Dr J B Woodman, president of the New Hampshire Medical Society, was present and spoke at length on the Wagner Bill.

After luncheon was served, two papers were presented. Dr Donald S King, of Boston, spoke on "Serum and Sulfapyridine in the Treatment of Pneumonia," and Dr Channing C Simmons, of Boston, gave a talk on "Some Points in the Diagnosis and Treatment of Cancer."

The twenty-eighth annual meeting was held at the Nashua Country Club, on April 16, 1940. The secretary, Dr D G Smith, told of the aims of the National Physicians' Committee for the Extension of Medical Service. Following a discussion by the members, it was unanimously voted to approve the committee and its work, that \$100 be given the committee and that copies of the resolution be sent to Senators Bridges and Tobey.

An amendment to the constitution was proposed by Dr Smith, making citizenship in the United States one of the necessary qualifications for membership in the Hillsborough County Medical Society. It was said that Dr Woodward, director of the Bureau of Legal Medicine and Legislation of the American Medical Association, had stated that the amendment would not conflict with the constitution and by-laws of either the New Hampshire Medical Society or the American Medical Association.

Dr Biron told of the effort of the American Society of Clinical Pathologists to curtail the activities of state laboratories.

After luncheon a 'Symposium on Arterial Disease' was presented by Drs Burton E Hamilton, Lawrence B Ellis and Reginald H Smithwick, all of Boston.

T F ROCK.

## Merrimack County

The Merrimack County Medical Society held four meetings during the past year.

On July 5, 1939, a meeting was held at the Franklin Country Club, with the vice president, Dr Frank H. McQuade, presiding. The speakers were Dr James B. Woodman, and Dr Samuel R. Detweiler, of Columbia University College of Physicians and Surgeons. Dr Arthur F Wright, of Bradford, was elected a member of the society.

On October 4, 1939, a meeting was held at the Eagle Hotel in Concord. Mr Lloyd C. Fogg, of the University of New Hampshire, spoke and showed slides on the subject, "The Effect of Irradiation on Tumors of the Breast." It was voted to request the Speakers' Bureau to furnish speakers to conduct public debates on the Wagner Bill if occasion should arise.

The new members elected into the society were F J Kropp, of Franklin, Seth F H Howes, of Concord, Herbert A Barnes, of Antrim, and John H Branson, of Concord.

On January 3, 1940, the annual meeting was held at the Eagle Hotel in Concord. In the absence of Drs. McQuade and Shields, Dr Dolloff was appointed acting president by the secretary. The following officers were elected:

President Frank J. McQuade, Franklin.  
 Vice-president MacLean J. Gull, Concord.  
 Secretary-treasurer Warren H. Butterfield, Concord.  
 Censors Joseph M. McCarthy (3 years) Concord  
 Harold D. Levine (2 years) Bristol and Concord  
 Henry H. Amsden (1 year) Concord.  
 Delegates Warren H. Butterfield, Concord Clarence  
 E. Butterfield, Concord Charles H. Parsons, Concord  
 William P. Clough, New London.  
 Auditors Philip M. Friesberg, Concord Walter C.  
 Rnwe, Concord

Dr. J. Kenneth McLeod of Penacook, was elected a member of the society and Dr. Ernest H. Jny of New Jersey was reinstated. Dr. Sibley Morrill was voted into affiliate membership. Dr. James B. Woodman spoke briefly on the Wagner Bill. Dr. John Wheeler of the State Board of Health discussed district public-health reorganization in New Hampshire.

On April 3, 1940 a meeting was held at the Eagle Hotel in Concord. Dr. James M. Baty of Boston, spoke on "Preventive Measures in Infancy."

It was voted to have the July meeting in Franklin on July 10, 1940.

HENRY H. AMSDEN

### Rockingham County

The Rockingham County Medical Society held two meetings during the past year.

The first was held at the Exeter Hospital and the second at the Portsmouth Hospital. At these meetings, various case histories were read and discussed and x-ray plates exhibited. Patients were presented to show the results of operation and treatment. Luncheon was served at the hospitals.

HERBERT L. TAYLOR.

### Strafford County

The Strafford County Medical Society had for the year 1940 28 active members and 6 affiliate members.

The annual meeting was held on October 5, 1939 at the American House in Dover. It was the one hundred and thirty second meeting of this society and was attended by 27 members and guests.

Dr. J. B. Woodman presented the problems of the New Hampshire Medical Society. Drs. C. W. McClure and L. R. Jankelson, of Boston, spoke on "Gastroscopy and Its Use in Differential Diagnosis."

The spring meeting is planned for April 17, 1940 at the American House in Dover at which Dr. I. J. Zimmerman, of Manchester will speak on "Infections of the Urinary Tract."

There were no deaths among the members during the fiscal year.

J. A. HUNTER.

### Sullivan County

The Sullivan County Medical Society convened four times during the past year each time in Claremont, and the occasion was marked in every instance by a good attendance. Two of these meetings were for purely business purposes, while the other two were devoted chiefly to the discussion of scientific subjects.

In the summer we were fortunate in having as our guest Dr. Percy S. Pelouze, of Philadelphia who talked on "The Treatment of Gonorrhea."

In the fall we were entertained at the Claremont General Hospital to which institution we are greatly indebted

for a most excellent luncheon. At this time we had the annual election of officers and a paper was read by Drs. Harry C. Sanders, Jr., and C. Carter Hamilton of Claremont, on "A Ray Diagnosis of Malignancy." Dr. Emery M. Fitch opened the discussion.

We were favored by the presence of Dr. James B. Woodman, who talked on the present-day problems of the New Hampshire Medical Society as well as those of the American Medical Association with special reference to the Wagner Bill and the proposed building of government hospitals in New Hampshire.

EMERY M. FITCH

DR. ROBERTSON: Your committee has reports from all the councilors, for the first time in many years, due to the untiring efforts of Dr. H. H. Amsden.

It recommends the adoption of these reports.

This motion was seconded and was carried.

SPEAKER FERNALD: Have there been any affiliate members voted upon in any counties?

DR. DEERING G. SMITH: The Hillsborough County Medical Society voted an affiliate membership to Dr. P. J. McLaughlin. I move that he be made an affiliate member of the Society.

This motion was seconded and was carried.

DR. BUTTERFIELD: I nominate Dr. Sibley G. Morrill of Concord, for affiliate membership.

This motion was seconded and was carried.

DR. ROBERTSON: I move that Dr. Elizabeth B. Reed, of Keene, be made an affiliate member.

This motion was seconded and was carried.

SPEAKER FERNALD: As the next order of business come the reports of the standing and special committees.

I should like to have a report from Dr. Henry O. Smith on the Special Committee for the Sesqui-centennial.

*Report of the Committee to Formulate Plans for the Observance of the One Hundred and Fifteenth Anniversary of the Society*

The committee recommends:

1. That the anniversary be observed in connection with the regular meeting of the Society in 1941.

2. That the sketch of the Society to 1854 which was prepared and read in 1891 by Dr. L. Bartlett How be edited, amended and brought nearer to date, that it contain a portrait of Dr. Josiah Bartlett and that it be printed for distribution to the members of the Society prior to the meeting.

3. That an exhibit of old medical books, instruments and other objects of interest be on display, that the Dartmouth Medical School be asked to co-operate in this exhibit, and that it be under the direction of Dr. Fred E. Clow.



4 That Rev William Porter Niles, son of Rt. Rev W W Niles, who offered the opening prayer at the meeting in 1891, be requested to perform that duty in 1941,

5 That on the evening of the first day of the general session, an entertainment be provided, under the direction of the Manchester Medical Society, but financed by the New Hampshire Medical Society,

6 That the literary program be given on the afternoon and evening of the second day of the general session,

7 That the selection of the speaker to give the chief address be made by the secretary of the Society,

8 That the presidents of the other five New England state medical societies be invited to give five minute talks,

9 That the appreciation of Dr Josiah Bartlett, pronounced by Dr Thomas W Luce, his final words to this society as its president, be read by Dr Marion Fairfield,

10 That a paper on "The Doctor of One Hundred and Fifty Years Ago" be prepared and read by Dr H. H. Amsden,

11 That a paper, "The Leaders of Old," be presented by Dr F E. Clow, and

12. That so much as may be required of the sum of \$1000 be placed at the disposal of the Secretary-Treasurer to defray the expenses of this observance.

HENRI O SMITH

DR ROBERTSON The Committee on Officers' Reports wishes to express its appreciation for the detailed plan presented by this committee

We recommend that this report be considered point by point

Each recommendation was seconded and was carried

### *Report of the Committee on Amendments to the Constitution and By-Laws*

No suggestions for changes in the constitution and by laws of the New Hampshire Medical Society have been submitted to your committee during the year. None have been originated by the committee.

FRED E. CLOW,  
LOUIS W. FLANDERS,  
PHILIP McQUESTEN

DR ROBERTSON The Committee on Officers' Reports notes the failure of the Committee on Amendments to the Constitution and By-Laws to compare our constitution and by-laws with those of the American Medical Association

I move the adoption of this report

This motion was seconded and was carried

### *Report of the Committee on Social and Mental Hygiene*

During the past year, from April 1, 1939 to April 1, 1940, 79 mentally deficient persons were admitted to Laconia State School, 5 were readmitted, and 49 discharged, 15 women and 6 men had legal sterilizing operations performed

The bed capacity of Laconia State School is 616, there are in the institution 640, and out on parole under supervision, 73, applications for admission from 13 males and 40 females are on file.

In a further effort to make room, some exchanges of older patients from the institution for younger and more trainable individuals have been made with the counties

In accordance with the marriage law, 50 children from the public schools were reported as feeble minded to the Board of Health by the Department of Education. It is stated that of the 400 children examined psychometrically in the Mental Hygiene Clinics of the State Hospital, 150 were found to be mentally deficient.

The insane, epileptic and feeble-minded persons of New Hampshire constitute a group on which there are no special statistics, they, therefore, compare unfavorably with lumber, highways, summer visitors and shoes, which are all statistically enumerated. There is no point of departure from which to report an increase or decrease per capita of population

Thirty-two patients with neurosyphilis were admitted to the New Hampshire State Hospital during the year 1939. A total of 307 general inductothermy treatments were given to 31 patients. Of this group, 19 patients had general paresis, 5 tabes dorsalis, and 4 interstitial keratitis and neurosyphilis, the others suffered from other types of neurosyphilis. Of the 31 patients treated, 21 were able to leave the hospital in an improved or recovered condition.

The State Hospital has been co-operating with the State Department of Venereal-Disease Control, whereby patients in the clinics can be referred to the State Hospital for neurological check-ups and spinal fluid studies. If indicated, arrangements have also been made for selected patients to receive fever treatment in the hospital. After completion of the fever treatment the patients are referred back to the clinics for follow up therapy

New methods of treatment in tabes dorsalis and paresis, which consist of combinations of intravenous, intraspinal and fever therapy, are being investigated at the hospital, with what appear to be promising results

Between April 1, 1939, and April 1, 1940, the State Hospital admitted 686 patients, 71 more than the previous year. Of these 193 were readmissions. Nevertheless, they contributed to the already overcrowded conditions. During the same period 571 patients were paroled and 382 were discharged

The State Hospital has kept abreast with modern psychiatric curative agencies, treatment with Metrazol was used in 163 cases. While some of the patients have lapsed after making marked improvement, many have been greatly benefited and some probably permanently relieved, showing this treatment to be a valuable aid in treating the mentally ill. Eight patients were given the legal sterilizing operation

The staffs of the Mental Hygiene Clinics of the State Hospital have examined and given helpful advice to 843 patients in four of the principal cities of the State. There has been some increase in the Social-Service Department personnel at the State Hospital and a second assistant physician has been added to the staff at Laconia State School

Both state institutions admit those suffering from the convulsive disorders. If in the future New Hampshire should have an institution especially designed and administered for the care of this class of patient, it would be in keeping with the best practices in many states. It would

relieve other institutions of a disturbing element and assure special care to those suffering from a most pathetic affliction.

The last Legislature made an appropriation for some reconstruction and some new construction. Plans and preparations are now under way looking toward the creation of needed general hospital facilities at the State Hospital and additional room at both institutions.

BENJAMIN W. BAKER,  
CHARLES H. DOLLOFF,  
JOHN B. McKENNA.

**DR. ROBERTSON** The Committee on Officers Reports deplors the crowded conditions in the two state institutions, and approves the establishment of a separate institution for the care of those suffering from convulsive disorders.

We ask the Committee on Social and Mental Hygiene to present plans for the enumerating of the mentally deficient at the next annual meeting.

I move the adoption of this portion of our report.

This motion was seconded and was carried.

#### *Report of the Committee on Control of Cancer*

Both the public and the physicians of New Hampshire are becoming more conscious of the early symptoms that may indicate cancer and this recognition is followed by earlier treatment.

There is still much room for improvement in both the attitude of the public and that of some physicians. The possibility of cancer in any growth in a visible location such as the skin or in the mouth seems to be quickly recognized by physicians, but unfortunately there are still needless delays in examining patients who bleed between periods after the menopause, and from the rectum and bladder. Women who are flowing abnormally should not be denied an examination on account of flowing.

The public is apparently reacting to the educational efforts of the Women's Field Army. Year by year more families are becoming aware of the danger due to neglect, and many more people are presenting themselves at doctors' offices for examination. We believe that physicians must do everything in their power to educate and advise the public regarding the curability of cancer with particular reference to the need of early diagnosis and early treatment. The Pathological Laboratory at Hanover gives us the encouraging information that more biopsies from early cancer are appearing from all parts of the State than ever before.

Active state wide efforts for cancer control did not begin until 1933 and it is to be expected that it will take about ten years of this activity before we can look for a drop in the mortality rate. We hope it may appear before that date.

A few years ago the State Board of Health made cancer a reportable disease for the purpose of ascertaining if possible, the number of existing cancer cases within the State. We regret the lack of co-operation among physicians in refusing or neglecting to fill out the simple yellow forms and sending them to the State Board of Health. These names are never publicized nor are the patients called on or contacted in any way as a result of their names being placed on file. We dislike to admit that a fairly accurate census of this sort has been impossible on account

of a lack of co-operation on the part of the physicians of the State.

During the past year the committee has sent out three letters to every physician in New Hampshire. As usual these letters have covered very briefly some important points in cancer diagnosis or treatment.

The first letter was sent out January 9 1940 and was devoted to a discussion of more careful diagnosis in cases of uterine flowing before any radical operation is considered. The second letter sent out in April was a further discussion of the same subject, and there were included brief histories of three cases that had occurred immediately after the previous letter where inadequate examinations had been made. The final letter was sent in May and briefly discussed malignant bone tumors. The committee continues to have occasional requests from other states for copies of these educational letters.

Your committee co-operates whenever necessary with the New Hampshire Cancer Commission and with the Women's Field Army of the American Society for the Control of Cancer.

We have spent, for printing and postage, \$44.32 of the \$50 appropriated. The balance, \$5.68 has been returned to the Treasurer and we request another appropriation of \$50 for the coming year.

GEORGE C. WILKINS,  
HOWARD N. KINGFORD  
GEORGE F. DWINELL.

**DR. ROBERTSON** The Committee on Officers Reports would emphasize the request for better reporting of cases of cancer to the State Board of Health. We recommend the appropriation of \$50 for the work of this committee.

I move the adoption of this portion of our report.

This motion was seconded and was carried.

#### *Report of the Committee on Maternity and Infancy*

In accordance with the practice of the past six years, the Committee on Maternity and Infancy has prepared an annual report on maternal deaths, infant deaths and stillbirths. This study as formerly was done in co-operation with the Division of Maternal and Child Health of the State Board of Health.

As a new activity this year the committee sent individual letters to the physicians reporting maternal deaths. Comments, suggestions and a report of the findings in each case were included in the letters.

As in the past, all information received was entirely confidential. Only one person had knowledge as to the identity of the physician, hospital or patient. That person was the Director of the Division of Maternal and Child Health, acting as agent for the committee in carrying on this study.

Six meetings of this committee were held. At each meeting the information collected was gone over carefully each case being studied from all possible angles. The material used consisted of a copy of the death certificate and answers to the questionnaire sent to the physician who reported the maternal death and in most cases, information was obtained by a personal interview between the agent of the committee and the physician in charge of the case. Wherever possible the hospital record was studied and the findings were included in the report to the committee.

tee The committee studied all cases by number. In each the letter sent to the physician was transmitted through the Division of Maternal and Child Health and contained only the decisions and opinions of the committee members.

Infant deaths and stillbirths were studied from answers to questionnaires and information obtained from the death certificates. These studies were obviously not so exhaustive as those on maternal deaths.

Statistics of the United States Bureau of the Census show that, on comparing the maternal death rates of 1934-35 with those of 1936-37, there was no significant change in the figures for New Hampshire. By this is meant of course that a lowering of the rate from 5.4 per 1000 live births in 1934 to 4.3 in 1937 is not significant from a statistical viewpoint. Nevertheless it is encouraging to note that there has been a downward trend in the rates from 1930 onward, from a rate of 6.2 to 3.1 in ten years. It is hoped that this downward trend will continue.

In 1939 there were 25 maternal deaths. The chief causes of death were found on analysis to be in the following order: toxemia of pregnancy, cesarean section, with complications, accidents of pregnancy, miscellaneous causes.

The committee is gratified to note that there are fewer cesarean sections being performed. It can be seen, however, that toxemias of pregnancy are still the greatest factor in maternal deaths in New Hampshire. There were 6 autopsies performed, which is an encouraging improvement over findings of the previous year, which showed only 2 complete autopsy records.

Twenty, or four fifths of the cases, were urban, and the greatest number of deaths occurred in Hillsborough County, where the largest center of population exists.

For the most part, hospital records were more complete than formerly, although there still remains much to be done by the hospitals in reference to requiring more adequate histories and records. A number of the hospitals required written consultations on cesareans, while others had no record of the operative procedure. Most physicians had prenatal office records on their cases.

It was found that the forceps is used too frequently, with apparent failure to distinguish between high, mid and low forceps application. There seems to be confusion in the use of terms in this procedure. The committee has repeatedly made recommendations in regard to forceps, namely, that high forceps be eliminated entirely, that mid forceps be eliminated so far as possible, and that forceps should not be applied until the head is on the perineum.

In the study of infant deaths under one year it was found that the rate was 39 per 1000 live births. This is lower than the rate for 1938, which was 48.

The committee believes that not enough autopsies are performed after the death of young infants. A true diagnosis is frequently obscure, especially in the newborn.

The number of infants dying under one year of age in 1939 was 307. From a study of causes it seemed obvious that prematurity was the chief cause of death. It was shown that it was the predominant cause of death for the first day, and that after this time it became, of course, less prominent. There was no record of the weight of the infant given on the certificate, so the accuracy of the diagnosis is uncertain. The variety of causes of death in the infant increased directly with the length of time the child lived. Toward the end of the first year the chief cause of death shifted from prematurity to bronchopneumonia. It is of interest to note that there were 9 infants

who died of suffocation. It is unbelievable that a preventable condition of this type should take that toll.

A study of stillbirths was made from an analysis of death certificates and from answers submitted by physicians to questionnaires. This study revealed that there were 211 stillbirths during the calendar year of 1939. The leading cause of death was given as prematurity.

As a result of these studies the committee recommends that there be an improvement of segregation of maternity patients from other patients in hospitals, that there be provision of isolation facilities for infected cases and that hospitals provide apparatus for resuscitation and for control of hemorrhage. Vaginal examinations should be performed during labor only under the strictest aseptic technic, and then only when labor is not proceeding normally. Rectal examinations should be done instead. The prevention of toxemias is to be attempted through thorough and vigilant prenatal care, but if symptoms do arise, therapeutic methods should be used which are recognized as effective.

The committee believes that there are still too many cesarean sections being performed in New Hampshire without clear-cut indications, without proper consideration of the facts in the case, and without competent consultation. The committee realizes that the question of indications for cesarean sections is a more or less controversial one, and that there is rarely an absolute indication. However, the committee believes that there are a few indications that are fairly clear cut. In general the committee believes that cesareans should not be planned until the onset of labor except in the following conditions: previous section, blocking of the inlet due to soft-tissue tumor or due to extreme bony deformity, and carcinoma of the cervix.

Fairly definite indications in which a section would be warranted as the condition arises in the last trimester of pregnancy or at the time of labor are as follows:

Excessive hemorrhage, placenta previa, especially in a central previa or in marginal previas where the bleeding is uncontrollable by other methods or by the descent of the head — it is the general consensus that the use of the Voorhees' bag is desirable, premature separation of the placenta, where hemorrhage is severe in a patient who has a partial or complete separation of the placenta and who is not in labor.

Marked disproportion, where the disproportion is evidently due to marked difference in size of the baby's head and the pelvic inlet, and then only after a reasonable test of labor has been tried. A test of labor is usually designated as labor which is accompanied by good pains at three to five minute intervals, which have been recurring for from six to eight hours, resulting in some dilatation of the cervix but no descent of the head. There is too frequently the tendency to early intervention by doing a section before the patient has had a chance to demonstrate the effectiveness of labor. This is particularly true in primiparas.

Toxemias of pregnancy. The committee believes that there is a definite place for cesarean sections in the delivery of cases that have not done well under proper treatment, chiefly in a primipara whose cervix is rigid and where there is a possibility of a disproportion, and where fairly rapid emptying of the uterus is necessary or desirable. In all cases of toxemias, multiparous or primiparous, where the head is low and where the cervix will permit the

rupturing of the membranes, the committee is certain that induction of labor by this means with delivery from below is desirable.

The committee repeats that too many cesarean sections are being done that should not be done unless there are sufficient indications, and then only under proper circumstances with written consultations recorded on the hospital records. This is also in accordance with the requirements of the American College of Surgeons.

The committee believes that physicians should not depend on making a diagnosis of disproportion by the use of a flat x-ray plate of the abdomen. There is no value whatsoever by such a procedure, and it may lead to a false sense of security. Clinical judgment in most cases is preferable. The committee does however recognize the value of newer methods of x-ray pelvimetry but recommends that this be relied on only when done by a competent radiologist.

The committee wishes to reiterate that an accouchement forc   done for any condition whatsoever is to be condemned. There is no justification for such a procedure under any circumstances.

The manual removal of a placenta is unjustifiable and there is no excuse for such a practice unless there is excessive and uncontrollable bleeding. If there is a retained placenta but the bleeding is not excessive, removal should not be attempted under twelve hours. The committee recommends that doses of 1 cc. of pituitrin be given at two-hour intervals, accompanied by the Cr  t maneuver only at the same time the pituitrin is given.

The committee recommends that chloroform be not used for deliveries or labor when ether can be obtained. It is a well-known fact that chloroform is more toxic and more treacherous than ether.

It is recommended that physicians attempt to secure autopsies on stillbirths in order that an accurate picture be obtained as to the cause of death. It is also desirable that autopsies be secured following infant deaths and maternal deaths when the cause of death is obscure.

Where hospital facilities are available it is strongly recommended that laboratory facilities be used especially in reference to blood counts, blood studies and cultures of blood and lochia. Where a puerperal patient has an elevation of temperature to 102 F., the lochia should be cultured immediately and be a routine procedure under such circumstances. Blood cultures should be taken if the temperature does not decrease in the twenty-four hours after onset.

The committee expresses its hearty appreciation of the splendid co-operation received from the physicians who answered questionnaires and received so cordially the agent delegated by the committee to secure the data. Also the committee thanks the hospitals that so generously co-operated especially those that have given evidence of taking former recommendations seriously enough to attempt improvement in facilities and technique concerned with obstetric patients and newborn infants.

To the Division of Maternal and Child Health of the State Board of Health the committee expresses its thanks for the efforts and detailed work performed in the preparation of this report.

ROBERT O. BLOOD  
BENJAMIN P. BURPEE,  
MARION FAIRFIELD.

DR. ROBERTSON. Your committee urges that all physicians doing obstetrics carefully peruse the statistics contained in this report and observe the recommendations.

I move the adoption of this part of our report.

This motion was seconded and was carried.

### *Report of the Committee on Medical Education and Hospitals*

The organization of the Associated State Committees on Postgraduate Medical Education has been perfected during the past year to a point which provides for a definite contact between the interests of the different state societies and the federal government in this field.

A meeting of representatives of each of the states has taken place at each annual meeting of the American Medical Association. Much of the spare work has been done, a fact which should result in some fair degree of co-ordination between the objectives of the different state societies and the equipment and funds necessary for the furtherance of this activity which the federal agencies seem to be interested in providing.

The New England Postgraduate Assembly will hold its third annual session on November 13-14. Its previous sessions have been regarded as most successful. There is the expectation that more publicity will be given than heretofore among members of the state societies. The attendance while good could and should be improved.

The Commonwealth Fund Fellowships are continuing to be offered. We still have what seems to your committee a woefully small appreciation of the opportunities as judged by the number of applications. The information was mailed to the membership of the Society in January and we have responded to fourteen requests for forms. Presumably these fourteen applications were made to the officials of the Fund. This is the identical number of requests that was made a year ago. There does not seem to be any available means of additional publicity or urging that has not already been used. It is also true that a considerable portion of these requests are repeats. In this connection it is interesting to note that probably the policy of the Commonwealth Fund is not to grant one man more than four appointments.

No attempt at enlargement of the Speakers Bureau was made for this year, it being the policy to correct and make additions to the list every second year as there are not enough new men coming into the State to make it practical as an annual revision. The list is in the hands of the secretary of each county society. It has been used to some extent through the committee and probably more often directly through the secretaries and therefore without our knowledge.

JOHN P. BOWLER,  
JAMES W. JAMESON,  
HARRIS E. POWERS.

DR. ROBERTSON. To make better use of the Commonwealth Fund, we recommend that the Committee on Medical Education and Hospitals, in its annual letter explaining the Fund state that fellowships are granted to physicians who do not come within the specifications as to age and location.

I recommend the adoption of this part of our report.

This motion was seconded and was carried.

(To be continued)

## REPORT ON MEDICAL PROGRESS

## KIDNEY DISEASE

REGINALD FITZ, M.D. \*

BOSTON

CERTAINLY, in one way or another, Goldblatt has fathered a great deal of significant work on cardiovascular renal disease during the past year, work that is interesting, be it at present chiefly of theoretic interest.

As one by-product, those with chemical leanings have resurrected "renin," originally described by Tigerstedt and Bergmann<sup>1</sup> in 1898. The studies of these investigators lay firmly buried for eleven years until Janeway<sup>2</sup> exhumed them in 1909, through a brief note on the rise in blood pressure which he observed following the reduction of renal arterial circulation in dogs after ligation of the renal arteries. And now once more, indirectly owing to Goldblatt's stimulation, the extraction and purification of renin from the kidney have come to occupy the minds of several investigators.

The techniques employed by various workers on the problem have varied, but the general plan has been to extract from renal tissue a blood-pressure-raising principle, to identify it and to study the manner in which it behaves. Prinzmetal, Friedman and Abramson<sup>3</sup> found that saline extracts of ischemic dog kidney and of kidneys of human subjects with hypertension yielded greater pressor effects than did similar extracts of normal kidneys. Helmer and Page<sup>4</sup> have extracted highly purified preparations of renin, as have Swingle, Taylor, Collings and Hays<sup>5</sup> and Merrill, Williams and Harrison<sup>6</sup>. All such work points inevitably to the conclusion that the kidney does, in fact, contain a pressor substance, although how important from a clinical viewpoint this may be is less certain.

Coming closer to the patient and incorporating Goldblatt's ideas is an ingenious bit of experimentation by Page<sup>7</sup>. He produced what he termed proliferative perinephritis in animals as a reaction to enclosing the kidneys in cellophane. Animals so treated developed hypertension, and removal of the kidney, when but one was so treated, cured the hypertension. Thus Page suggests that besides unilateral pyelonephritis with ischemia as a curable cause of hypertension, unilateral perinephritis may be another.

From a strictly clinical angle there are now on record numerous case reports of "Goldblatt men" removal of whose unilateral ischemic kidneys has seemingly cured hypertension. Thus Goldblatt's work is now established on a firm clinical footing.

Today, the hypertensive individual who requires meticulous study deserves careful scrutiny from the combined talents of internists, urologists and radiologists. On the other hand, to prevent undue enthusiasm and unnecessary surgery, the warning of Schroeder and Fish<sup>8</sup> is worth emphasis. In their experience, the removal of a single diseased kidney for hypertension is likely to be of lasting benefit only in patients in whom the existence of hypertension is of short duration, and in whom arteriolar sclerosis of the other kidney is not advanced.

Approaching Goldblatt's work from another angle is a case reported by Derow and Brodny<sup>9</sup>. This patient had a congenital lesion of the posterior urethral valve, producing obstruction and, eventually, the clinical picture of renal rickets. Carey<sup>10</sup>, too, emphasizes the potential importance of urinary infection, as did Weiss and Parker<sup>11</sup> a year ago. Neglected cases of pyuria and urinary infection in children, he says, may result later in severe renal damage and perhaps, too, in hypertension. The preventability of certain cases of chronic nephritis with hypertension by careful urological investigation and early treatment of urinary infection or obstruction is a recent concept most important to bear in mind.

Unusual forms of kidney disease not ordinarily encountered are always worthy of mention. Several months ago two papers appeared at about the same time re-describing what Kimmelstiel and Wilson<sup>12</sup> in 1936 termed intercapillary glomerulosclerosis. Newburger and Peters<sup>13</sup> from New Haven reported 4 autopsied cases with this lesion and 5 additional cases which were characteristic clinically. Derow, Altschule and Schlesinger<sup>14</sup> from Boston reported another autopsied case. As one reads these two papers and compares the photographs which reproduce the glomerular lesions characteristic of this condition, it is clear that both teams of observers were describing the same type of case. The clinical earmarks of the patient with this peculiar glomerular lesion are readily distin-

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guishable. The constant features of the disease are a combination of diabetes, albuminuria, hypertension and retinal vascular changes. The nephrotic syndrome is common, and depends for its development on the extent and duration of the albuminuria and the protein intake. The pathogenesis of the condition appears to be a severe and extensive arterial and arteriolar degeneration associated with and perhaps resulting in diabetes mellitus, hypertension and renal damage. Differential diagnosis requires among other lesions the exclusion of amyloid disease coincident to diabetes and hypertension—a rare combination which might conceivably reproduce this syndrome.

Anyone with experience in diabetes is likely to recall cases of intercapillary glomerulosclerosis, since its clinical features are so striking. Unless one has the disease in mind, however, it will pass unnoticed. Further knowledge concerning so notable a diabetic renal lesion is desirable.

Another familiar form of renal disease which needs continual emphasis has been well discussed recently by Thompson, Frazier, and Ravdin.<sup>18</sup> These authors have studied the renal lesion in obstructive jaundice. At times, as is well known this terminates with what surgeons are apt to call the "hepatorenal syndrome." Basically, the renal disturbance in obstructive jaundice, according to the experience of these investigators, appears to be a tubular lesion where the tubules are dilated and show compression of the lining epithelium with areas of vacuolization, fragmentation or desquamation. Thompson, Frazier, and Ravdin point out that if no previous renal injury exists, the evidences of cholemic nephrosis are likely to disappear quickly following the release of the obstruction. On the other hand, in fatal cases, glomerular changes are likely to be found, being due they presume, to a pre-existing renal disease. Since the hepatorenal syndrome is such an uncomfortable condition to contend with in one's patient who has obstructive jaundice and who comes to operation, it is worth remembering beforehand that in liver disease with jaundice the condition of the kidneys is important, and that patients with a known renal lesion may do badly following operative procedures for the relief of obstructive jaundice.

Prather<sup>16</sup> has published a timely paper. As he says, "with the present adult public addicted to fast driving and the modern juvenile population actively engaged in individual and scholastic athletics during all months of the year, it is not surprising that patients with injuries to the kidneys are often encountered."

All doctors, nowadays, should know something of traumatic conditions involving the kidneys.

Prather reviews 20 cases. The types of renal injury which he met most often were contusions of the kidney, subcapsular rupture, laceration of the kidney and its capsule, and severance of the renal pedicle. Of course, in any given case, the trick is to make an accurate diagnosis and determine the best form of treatment.

Prather advocates, as an aid to diagnosis, pyelographic studies by the intravenous method shortly after the patient is seen and, naturally, careful examination of the urine, above all, careful examination of the patient, his blood pressure level, his pulse rate and his body temperature. Pyelographic studies, as judged by the illustrations in Prather's article, are likely to yield a great deal of valuable information. It is surprising too, how many of his patients with serious renal trauma recovered without operation. In this particular field of kidney disease it is obvious that well organized team play between the internist, the urologist and the radiologist is indicated. An error in therapeutic judgment is likely to prove costly to the patient.

Madding, Binger and Hunt<sup>17</sup> report a case with another unusual form of kidney disease, acute urinary suppression which developed postpartum. The patient was a primipara. Immediately after delivery she became almost completely anuric for eight days. No urologic lesion was discoverable to explain the anuria, hence pregnancy was assumed to be the cause.

If this woman had symmetrical cortical necrosis of the kidneys, as is suggested the fact that she recovered is an unusual state of affairs, for of course the prognosis in cortical renal necrosis is almost hopelessly grave. She was treated by the liberal use of fluid, with 10 cc. of aminophylline given morning and afternoon, and by good nursing. In addition, she was given a diet low in protein, salt and condiments. Madding, Binger and Hunt believed that to use the more powerful mercurial diuretics was contraindicated on the ground that they might well have hindered the improvement that was taking place. Renal decapsulation was contemplated, but the procedure was dismissed as being too hazardous and as offering too slight an advantage to be attempted.

The treatment which was carried out so successfully in this case under circumstances where there must have been a very acute underlying renal lesion is interesting in the light of some experiments by Addis and Lew<sup>18</sup> and by Bergman and Drury.<sup>19</sup> The former, employing their "reversible acute uremia" in rats, found that none of the animals died when they were given diets low in protein, whereas the mortality was appreciably

higher when high-protein diets were employed. This fact they attributed in part to the potassium in the meat. Bergman and Drury, employing as an indicator the survival time in nephrectomized rats after different types of diet, also found that meat fed immediately before operation was definitely toxic, and they too concluded that potassium was harmful and responsible for part of the toxicity of meat. In the treatment of acute nephritis with anuria, therefore, the potassium content of the diet seems to deserve consideration.

Merrill<sup>20</sup> reports 3 cases of leukemia which tend to show the unpleasant effects on the kidney that may follow x-ray therapy. He says that uremia is not a rare complication of the x-ray treatment of this disease—a fact worth remembering. He believes that, since radiation in leukemia may bring about an enormous increase of uric-acid production within the body, and since such rapidly mobilized uric acid must be excreted by the kidney, such an increased burden may precipitate clinical uremia if the kidneys are sufficiently damaged either by leukemic infiltration or by non-leukemic lesions. He believes also that through radiation there is a danger of the formation of uric acid stones anywhere along the genitourinary tract. With these facts in mind he suggests that before treatment is instituted in leukemia preliminary studies of the blood levels of nonprotein nitrogen and uric acid are indicated, that during x-ray treatment a low-purin diet with large quantities of fluid should be employed, and that administration of alkalis by mouth, in an attempt to keep the urinary reaction alkaline and hence lessen the danger of uric-acid stone formation, should be instituted. This reasoning appears sensible.

Several papers have appeared during the year which emphasize the importance of the renal lesions that may develop from the use of sulfanilamide or its derivatives. Tsao, McCracken, Chen, Kuo and Dale,<sup>21</sup> Carroll, Shea and Pike,<sup>22</sup> Stryker,<sup>23</sup> and Scurry and Wittenborg<sup>24</sup> all report cases which, following the administration of sulfapyridine, developed hematuria. Several of their cases became anuric. In the fatalities that are reported, the necropsy findings were much the same. The striking findings were an acute nephritis and the precipitation of small calculi in sufficient quantity to cause obstruction to renal outflow. These cases bring forward additional evidence to suggest that when a patient is receiving sulfapyridine an abundant fluid intake is indicated, that hematuria should always be carefully looked for, and that when hematuria occurs it is a sign ominous enough to warrant the discontinuance of the drug. If anuria develops, ureteral catheterization and ir-

rigation of the renal pelvis may be a useful procedure.

What may be termed clinical stupidity in the management of renal disease has received several warnings. Quinby and Austen<sup>25</sup> report 4 cases which temporarily became anuric following too rapid a combination of intravenous and retrograde pyelography. That anuria lasting as long as seventy-six hours, as it did in one case, can occur after pyelography is worth emphasizing in these days, when the pyelographic method is being frequently used. Apparently what happened was that in sufficient time between the two tests was allowed to elapse and that pyelographic mediums were used in an amount too large to be passed successfully through a normal single kidney. Quinby and Austen issue a wise dictum. In cases in which there is reduction of normal renal function it is well to repeat pyelographic studies, especially by both the excretory and retrograde methods, only after at least a forty-eight-hour interval. In other words, overenthusiasm in one's zeal quickly to obtain accurate urological diagnosis may lead to trouble.

Anderson and Bethea<sup>26</sup> remind us that hypertonic solutions of sucrose injected by vein may by no means be innocuous. In 6 cases receiving such injections they found destructive renal lesions similar to those observed in experimental animals. Thus, they warn that the administration of hypertonic solutions of sucrose to patients with renal damage, whether to reduce intracranial pressure or as a diuretic, is inadvisable. Certainly large or repeated doses of this substance should be avoided.

Even the giving of too much salt solution in an effort to get rid of the dehydration that sometimes is seen in chronic nephritis may be harmful rather than beneficial. Evans and Shulman<sup>27</sup> show that if a patient is malnourished and with hypoproteinemia, this latter fact constitutes a contraindication to the administration of large amounts of salt and water parenterally. The taking of too much salt and water precipitates edema already potential by reason of a lowered osmotic tension, and hydremic plethora so induced further conditions the organism for the precipitation of an acute pulmonary edema. In the management of nephritis and fluid intake, therefore, the concentration of plasma protein is significant. Rare judgment may be necessary when it comes to deciding in a given case whether more or less fluid intake is indicated. The giving of too much fluid is fully as bad as that of too little, all of which goes to prove that good clinical judgment in the management of renal disease continues to be as necessary as ever.

Concerning the more general problems of nephritis and hypertension, Schroeder and Steele<sup>22</sup> have attempted to classify so-called essential hypertension. They have divided their cases into five groups. They believe that the origin of hypertension may be renal, nervous, endocrine, vascular or unclassified. Their paper is of especial interest in connection with one by Rennie,<sup>23</sup> who discusses the role of personality in certain hypertensive states. Admitting, with Schroeder and Fish, that many patients with hypertension have a nervous element behind their difficulties Rennie's ideas are sound. For he says that failure to recognize the personality component in hypertension may lead to serious complications and invalidism or elevated blood pressure, whereas willingness to deal with the personality features may offer the only or the most effective therapeutic tool. It is satisfying now to have clothed in elegant psychiatric language what older clinicians have known and taught for many years.

The advances during the year in the medicinal treatment of hypertension and chronic nephritis have not been striking. Mosenthal<sup>24</sup> has written an excellent article full of common sense, in which he says that since there are no means by which an elevated blood pressure can be appreciably and consistently lowered, the medicinal treatment of hypertension has resolved itself into the establishment of the most perfect possible physical and mental control of the patient. Of the drugs which may be of help, the barbiturates are as useful as any. The so-called vasodilators and tissue extracts which from time to time have been endorsed are not particularly satisfactory.

The usefulness of sulfocyanate is still under fire. Robinson and O'Hare<sup>25</sup> conclude that the drug in uncomplicated vascular hypertension in patients under sixty years of age, when carefully controlled has decided value. On the other hand Garvin<sup>22</sup> reports 8 fatalities following its use. Hamilton,<sup>23</sup> employing the experimental approach, has ingeniously made a study on the blood pressure level of street dogs. Sulfocyanate did not produce a significant or permanent lowering of blood pressure in such animals as were found to have hypertension. On the whole, the popularity of sulfocyanate

for the treatment of hypertension appears to be on the ebb.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 26301

#### PRESENTATION OF CASE

A forty-four-year-old bricklayer was admitted to the hospital complaining of a chronic cough.

The patient was a Turkish-born Armenian who spoke English so poorly that the history obtained from him was sparse and perhaps incomplete. He apparently enjoyed good health until two years before admission, when he caught a severe "cold" which left him with a residual dry, hacking, painless cough which was non-productive except for an occasional raising of small amounts of white phlegm. There was no admixture of blood at any time. Slowly over a period of months the cough improved and he gradually resumed work. It was stated that the cough appeared to be worse in winter and better in summer. Despite a good appetite he lost considerable weight. Ten weeks before admission he felt worse, becoming weak and tired. He stopped work and stayed at home, where he rested, with some improvement. His weight had dropped from an original of 140 pounds to 100 pounds. He noted increasing malaise and easy fatigability, and for a period of two weeks, approximately two months before admission, he experienced severe repeated night sweats but noted no other symptoms. Five weeks before admission he entered an outside hospital where x-ray studies of his chest were made. He was not informed as to their diagnostic import and was referred to this hospital for further diagnosis and treatment. On admission here he stated that his cough still persisted. He knew of no tuberculous contacts, and no one else in his family had experienced any similar ailments. There were no other complaints. The remaining family, marital and past histories were non-contributory.

Physical examination revealed a small man with a dry, hacking cough. The skin was loose and inelastic, and gave evidence of recent weight loss. Expansion of the lungs was limited bilaterally because of severe paroxysms of coughing incident to deep breathing. There was very slight dullness over the right base posteriorly, and a few loud rhonchi to auscultation. Tactile fremitus and voice sounds were normal over the area. The remainder of the chest examination was nega-

tive, as was the examination of the heart. The blood pressure was 120 systolic, 80 diastolic. The remainder of the physical examination was negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 5,700,000 with 95 per cent hemoglobin (Tallqvist), a white-cell count of 17,000 with 80 per cent polymorphonuclears, and a normal smear. Examination of the urine was negative. The sputum examination was negative for acid fast bacilli. Roentgenograms of the chest showed a sharply defined, rounded shadow in the right base filling the costophrenic angle. The septum between the upper and middle lobes was displaced slightly downward. The lower septum was not seen. In the lateral view the density was seen to lie posteriorly in the lower lobes. It was somewhat triangular in shape with its apex toward the hilus. The right upper lobe and the entire left lung were clear. The heart shadow was thought to have been slightly displaced to the right, but the diaphragm was normal in position. There was Lipiodol in many of the alveoli of the right lower lobe. After bronchoscopic examination and Lipiodol injections, which showed no definite findings, save obstruction to the right lower-lobe bronchus, it was observed roentgenologically that the upper posterior half of the right lower lobe did not contain Lipiodol and that the main bronchus to this portion of the lung had not filled. There was a suggestion of a pressure defect on the posterior surface of the main bronchus to the right lower lobe. This bronchus appeared narrowed, but there was a good filling of the bronchi to which it connected. There was still some air in the bronchi of the collapsed portion of the lower lobe, and a few flecks of Lipiodol, probably resulting from the previous injection in the outside hospital, were also noted. The middle lobe was unusually large, and there appeared to be two separate branches originating from the main right bronchus about 2 cm. apart, with evidence that the pressure on the right lower-lobe bronchus was most marked at the point of origin of the second branch.

He was discharged home for a six weeks' interval and returned to the hospital for operation.

#### DIFFERENTIAL DIAGNOSIS

DR. DONALD S. KING. We are told that the history is incomplete. There was a dry cough off and on for two years, with fatigue, a 40-pound weight loss, no pain, no hemoptysis, no purulent sputum, and night sweats for two weeks only.

There were a few loud rhonchi, but we are not told whether they persisted. Of course the presence of persistent unilateral rhonchi would mean partial bronchial obstruction, which is an important finding.

I do not agree entirely with the interpretation of the x ray films as given in the abstract, and I believe that there is at least one film missing I should like to put up the x ray films and discuss them with the roentgenologists. In the first place, we have a peculiar shadow in the cardiophrenic angle, not the costophrenic angle as reported. I believe that this shadow looks more like collapsed lobe than tumor, but it has a rounded border and is not the triangular shadow of a typical collapsed lower lobe. We discussed this case at the Thoracic Clinic, and Dr Churchill suggested that an injected lobe trying to expand as a result of partial bronchial obstruction would be of this shape.

DR. AUBREY O HAMPTON I remember that Dr Churchill propounded that theory. I did not believe it was necessary to suppose that the lower lobe was trying to expand. Why not a collapsed and water logged lobe?

DR. KING Would a water logged lobe give that shadow?

DR. HAMPTON I do not see why it should not.

DR. KING Is the entire lower lobe collapsed or only part of it? I am particularly interested in a study of the interlobar septums. The septum between the upper and middle lobes is obvious, and in the lateral film taken at the time of the first admission there is a septum shown between an upper and a lower lobe posteriorly. I am anxious to have Dr Hampton's opinion as to whether this is the septum on the right side or the left, because if it is the one between the right upper and lower lobes, there is a portion of the right lower lobe which is not collapsed.

DR. HAMPTON I believe that this is the septum on the left side and that the entire right lower lobe is collapsed. Otherwise we should not have the rounded shadow.

DR. KING The lateral film taken at the second admission would bear out Dr Hampton's contention because in this film the supposed septum between the left upper and lower lobes is not present, and the septum between the upper and middle lobes on the right side is displaced downward in a sharply rounded curve.

The next questions are whether there is some air in the collapsed lower lobe and whether bronchiectasis is actually present. I believe from the x ray interpretation that air is present. I should

guess from the plain films that there was evidence of bronchial dilatation. Do you agree with this Dr Sosman?

DR. MERRILL C SOSMAN I do not believe you can say because they are not filled with Lipiodol.

DR. KING You would not want to make a diagnosis without Lipiodol injection?

DR. SOSMAN No.

DR. KING Dr Hampton has often made the diagnosis before Lipiodol filling. What about this case, Dr Hampton?

DR. HAMPTON I agree with Dr Sosman, you cannot make a diagnosis of bronchiectasis unless you can see the dilatation better than you can here.

DR. KING You would not say that there is bronchiectasis from this film?

DR. HAMPTON No.

DR. KING As I said before, I believe that one of the oblique films taken after Lipiodol was injected is missing. In the films that we have I can see no evidence of two separate bronchi to the right middle lobe, and we are greatly confused by the fact that no oblique film was taken with only a right sided injection. It is impossible in these lateral films, it seems to me, to separate the bronchi of the left lower lobe from those of the right lower lobe. The report states that the bronchus to the right lower lobe appeared narrowed but that there was a good filling of the bronchi with which it connected. As I look at these films I can find no evidence of filling of any of the branches to the right lower lobe.

DR. HAMPTON I admit that confusion arises over the injection of the left side. All the bronchi are projected on this area which makes it more difficult. I interpreted this film. I remember that I studied it for quite a long time, and I think I must have had more films. Dr Adams helped me interpret it on the basis of the anatomic variation of the middle lobe that he saw at bronchoscopy.

DR. KING I take it then that the roentgenologists are willing to agree that there is collapse of the entire right lower lobe, and no Lipiodol filling of the bronchial branches to this lobe.

The final question concerns the evidence for a mass pressing on the right lower lobe bronchus. Personally I cannot make out such a mass and am not sure that there is a narrowed bronchus on the right side. I see the area in question, but it does not seem to me to have the density that one would expect from a tumor mass.

DR. SOSMAN I believe there is a mass in this region either collapsed lobe or tumor. The shadow is denser than normal.

DR KING Would you say that it was a mass and not an atelectatic lung?

DR SOSMAN Atelectatic lung is a mass "Shadow" would be a better term perhaps

DR KING I am still not convinced that there is x-ray evidence of a mass pressing on and narrowing the bronchus to the right lower lobe

The next focus of study is the bronchoscopic examination. The report in the abstract seems to me ambiguous. We are told that there were "no definite findings save obstruction to the right lower-lobe bronchus." It is very important to know more about this obstruction. Did the bronchus appear to be obstructed by a tumor mass or was the appearance that of an inflammatory process? Was the obstruction partial or complete, and was there bronchial secretion? Could a biopsy specimen be taken?

DR BENJAMIN CASTLEMAN I shall read the bronchoscopy report

The larynx, vocal cords and trachea were normal. The cricoid was blunt, and the left main bronchus came off at a right angle. The mucosa at the cricoid was normal. The right upper-lobe orifice was normal. Immediately below the right upper-lobe orifice the bronchus became narrowed to half its size. The middle-lobe orifice was pushed backward and was a direct continuation of the right main bronchus, so that at first it was thought to be the latter. Further examination, however, eventually demonstrated, far posterior to its usual location, an almost completely stenotic lower-lobe bronchus so narrow that only an aspirator could be introduced into it. No outcropping was seen. A moderate amount of secretion was obtained with the aspirator, but its odor was not foul.

Evidently it was not possible to obtain a biopsy.

DR KING My final conclusion is that we have complete obstruction of the right lower-lobe bronchus and collapse of the entire right lower-lobe, with some air remaining. We are then faced with the problem of what is obstructing this bronchus. The possible causes of bronchial obstruction are, of course, inflammation from tuberculous or non-tuberculous infection and tumor, either benign or malignant. The history of fatigue and weight loss makes one think of a malignant process, but there is nothing in the bronchoscopic examination or the x-ray studies which seems to me to prove this diagnosis. Neither is there evidence of tuberculosis. I believe, therefore, that we are dealing with an inflammatory stenosis of the right lower-lobe bronchus and that bronchiectasis is present in the atelectatic lobe.

DR CASTLEMAN Dr Sosman, would you venture a diagnosis?

DR SOSMAN Partial stenosis of the lower-lobe bronchus cause undetermined

DR RICHARD H SWEET We were unable to go

any farther with the preoperative diagnosis than Dr King has here. The discussion about the shadow in the right side of the chest, which has been interpreted here today as being that of an interlobar septum, interests me because at the operation it was obvious that there was no such septum. On opening the chest we found that the upper lobe had expanded and completely surrounded, except on the mediastinal surface, the collapsed and rounded lower lobe so that the lung markings which one sees even in the lower portion of the chest lateral to the lower-lobe shadow are those of the upper lobe.

The exact nature of the lesion was difficult to determine even when we were able to palpate it directly through the open wound. It was not possible to tell whether we were dealing with an inflammatory process or with a neoplastic one, or possibly a combination of both. The middle lobe, as well as the lower lobe, was atelectatic. We cut down on the tissues around the hilus and found after painstaking dissection that it was impossible to separate the upper-lobe structures because of involvement at that point with the disease process, whatever it might be. It was therefore obvious that we could do only a total pneumonectomy. This course was decided on, but in cutting across the hilar structures it was immediately obvious that we were dividing tissues which were involved in a pathologic process, although it was impossible to determine even then whether it was chronic inflammatory thickening or infiltration with carcinoma.

We knew when we reached that stage that we were cutting through pathologic tissue. Dr Bralley asks, what was the sense of continuing the operation, but having gone that far you cannot retrace your steps. He had an uneventful recovery and went home feeling well.

The most interesting thing about this case was the peculiar shadow, which was correctly interpreted by Dr Churchill and shown by the exploration to be caused by the collapsed and infiltrated lower lobe with the upper lobe completely surrounding it.

DR KING The middle lobe was collapsed at operation?

DR SWEET Yes, when we finally got to it seven weeks later.

#### CLINICAL DIAGNOSES

Bronchostenosis

Carcinoma of bronchus?

#### DR KING'S DIAGNOSES

Inflammatory stricture of the bronchus  
Bronchiectasis

## ANATOMICAL DIAGNOSIS

Epidermoid carcinoma of the bronchus of the right lower lobe.

## PATHOLOGICAL DISCUSSION

DR. CASTLEMAN I examined the specimen in the operating room and before cutting into the obstructing lesion was also in doubt as to its exact nature. A cross section through the main lower lobe bronchus showed that it was completely obstructed by a yellowish white granular tumor mass which involved the complete circumference of the bronchus and which extended outside the bronchial wall to form a tumor approximately 4 by 3 by 2 cm. The tumor extended along the bronchus for a distance of 4 cm., and definite tumor was present at the resected edge. Dr. Sweet was forced to cut through tumor in removing this lower-lobe bronchus because it extended almost to the main stem. There were metastases to the regional nodes around the main bronchus. Histologically it proved to be an epidermoid carcinoma, Grade III. There were atelectasis and fibrosis of the parenchyma of the lower lobe, but no bronchiectasis. The middle lobe was partially collapsed and the upper lobe was well aerated.

## CASE 26302

## PRESENTATION OF CASE

A twenty-four year-old carpenter was admitted to the hospital complaining of intermittent pain in the back.

The patient stated that he had experienced generalized backache occurring in three separate episodes, each lasting several successive nights, during a two-year interval prior to admission. The pain was always noticed as he retired to bed. He thought that it was a consequence of the strenuous physical work of his trade. Seven weeks before admission he "bumped" his back against a nail without breaking the skin, and noted a slight, local, transient pain at the point of contact. Two weeks later, however, on retiring to bed, he had a recurrence of the back pain experienced before the local injury. Its exact localization was not stated. It recurred on successive nights, and on the third evening was severe enough to awaken him from sleep. He arose from bed, and in so doing, accidentally struck the back of the left mid-chest region, where the pain was located. As he did this, he fainted, and the following morning he noticed local heat with swelling over the area. He rested at home for one week, then returned to work for about

ten days, during which time he experienced only slight discomfort over the "slight lump" which had persisted. The area caused no real pain unless he moved suddenly in bed or struck it while working. Nine days before admission trauma to the swollen area caused him to "nearly faint", he became nauseated and weak for several seconds. Since then he had experienced generalized weakness and attacks of vertigo and had fainted on at least two occasions. An x-ray examination of the painful area, made in an outside hospital, was said to have shown "inflammation of the bone." The pain steadily increased, and the swelling became larger. He was treated with chest strapping and rest, but because he failed to improve was referred to this hospital for further diagnosis and treatment.

The family marital and past histories were non-contributory.

Physical examination revealed a fairly well developed and well-nourished man whose face and upper back were covered with comedones and an acneiform eruption. There were small pimples in the skin of the chest that had previously been the site of adhesive strapping. A warm tender, fusiform swelling of the body of the left tenth rib was observed, without redness of the overlying skin. The remainder of the physical examination was negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 5,200,000 with 15 gm of hemoglobin (photoelectric-cell technic) and a white-cell count of 10,200 with 65 per cent polymorphonuclears, 21 per cent lymphocytes, 8 per cent monocytes and 6 per cent eosinophils; the smear was essentially normal. The urine was negative save for the sediment which showed rare red and white blood cells. Testing the urine by heat, nitric acid and alcohol for Bence-Jones protein was negative. The serum calcium was 107 mg per 100 cc., and the serum phosphorus 40 mg. The serum protein and nonprotein nitrogen were 6.8 gm and 23 mg per 100 cc. respectively. A blood Hinton test was negative.

Roentgenograms of the chest showed that the lung fields were clear. There was no evidence of mediastinal masses. The left tenth rib showed moth-eaten bone destruction of the inferior margin over an area 4 cm in length. There was very little thickening of the soft tissues, with no evidence of involvement of the pleura or of pericostal proliferation. The rib was not enlarged.

X-ray films of the kidneys were essentially negative by flat plate and intravenous pyelography.

In the flat abdominal film there was an increase in density and slight bulging of the right psoas muscle opposite the right kidney pelvis. Films of the spine, pelvis, femurs and skull were normal.

On the fourth hospital day an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR. CLIFFORD C. FRANSEEN: May we see the x-ray films?

DR. AUBREY O. HAMPTON: There were examinations of the skull, pelvis, spine, ribs, urinary tract and lungs, and the only positive findings are those mentioned in the record, except that in addition to the suggestion of a soft-tissue mass in the region of the psoas muscle there is also a suggestion of pressure on the kidney pelvis in the same area. In other words, there is some evidence that there might be a mass there. The psoas muscle, however, is still distinct.

DR. FULLER ALBRIGHT: Will you point out the rib defect?

DR. HAMPTON: It is here in this area. There is no new-bone formation, it is a purely destructive lesion without obvious soft-tissue mass or evidence of pleural disease.

DR. FRANSEEN: The first thing of importance is that this was a two-year history, so that we have to think of something that might have lasted over this period of time. There might be a coincidental condition to cause the backache. He bumped his back without breaking the skin and noticed slight pain as anyone might. He bumped it a number of times later, and it seems obvious that the area was hypersensitive, and that is why he seems to have bumped it so often. But he must also have had some systemic disturbance, because he fainted so many times, and he did not recover even with rest. He often had nausea because the pain was so severe. The generalized weakness and the attacks of vertigo certainly suggest some condition which was weakening him and undermining his general physical condition, he was apparently a strong twenty-four-year-old carpenter before his illness began.

A previous x-ray examination — we are not told how long before admission it was taken — showed inflammation of the bone, presumably some destructive process.

On physical examination he had the swelling over a rib. In view of the possibility of hypernephroma, it would be interesting to know whether this mass pulsated, but nothing is said about that.

We are helped but little by the laboratory work.

The slight leukocytosis might be accounted for on the basis of tumor or inflammation, in regard to the former, metastatic bone lesions, particularly those of hypernephroma, and a Ewing's tumor are both apt to give a leukocytosis. I cannot explain the 6 per cent eosinophilia on the basis of the bone lesion. The urine showed rare red and white blood cells, a finding which may or may not have significance. If a mass outside the renal pelvis or a neoplasm within was producing the red cells, they would be of importance in our diagnosis. No Bence-Jones protein was found, they were obviously looking for evidence of myeloma, although this protein has been reported in other conditions. The serum calcium and phosphorus at the levels given do not help either way. The serum protein was determined because its level is valuable in the differential diagnosis of multiple myeloma. Nothing is said about the phosphatase, but I doubt if it would have helped in this case. Metastatic lesions in our experience have always given a normal phosphatase if there is only a single lesion. There is nothing in the laboratory data which gives any lead to a metabolic disturbance of the bone, which this lesion might conceivably represent. The x-ray film is purely that of a destructive lesion, there was no periosteal proliferation. That is of diagnostic importance. The other important thing is the mass medial to the kidney. This might be a projection of a tumor from the kidney, an extraneous tumor lying medial to it or a tumor arising in a rest contiguous with the kidney. These are the things we must take into consideration in explaining both lesions with one diagnosis.

We have no lead whatever to a metabolic disturbance of bone in this case. The Hinton test was negative. It is difficult to believe that this was a chronic osteomyelitis going on for several years without any new-bone formation. It would be difficult to make a diagnosis of tuberculosis, on the basis of the evidence given here, as this mass in the region of psoas, if it had gone on for two years, should show some calcification, and certainly there is none in the x-ray film. In any event there should have been a new-bone formation.

We come to consider a neoplastic process, either primary or secondary. For primary neoplasm we have nothing to lead us to believe that this is a myeloma. The fact that it was a single lesion is against the diagnosis. Myeloma may occasionally not be demonstrable by x-ray and can give chronic pain in the back for a long time. Two years is a long time, of course, for any neoplastic process, but it can occur. Osteogenic sarcoma

would be extremely rare in a rib at this site. Lymphoma could give a destructive process like this. The rib lesion might be a metastatic lesion from the retroperitoneal mass, but we have no further evidence for considering that. When we come to secondary lesions, the appearance is not characteristic of a Ewing's tumor, but the diagnosis might remotely be considered. It would of course, be characteristic of carcinoma however we must look somewhere for a primary tumor. If we do that in a man of twenty four we have to consider everything in the gastrointestinal tract from the esophagus to the rectum. Certainly in the genitourinary tract a tumor arising anywhere from the kidney to the bladder and prostate may metastasize to bone. Even the pancreas has to be considered, but we have no lead. The only suggestion we have, of course, is the mass in the kidney region.

The insidious character of the metastases of those tumors from the kidneys which we commonly call hypernephromas is well known even after removal of the primary tumor, it may be ten years before metastasis to bone appears. It may give a purely destructive single lesion such as this is. It may pulsate, as Dr. Simmons and others have pointed out, because of extreme vascularity. The rare red blood cell in the urine might be related to the presence of such a tumor, and if I take the evidence at hand and make a diagnosis from that, I shall have to say that the working diagnosis for biopsy in this case is metastatic hypernephroma.

DR. HAMPTON: I might add that a tumor of the kidney that produces a pressure defect on the medial aspect of the kidney pelvis is rare. A papillary tumor of the pelvis is a possibility, but there is nothing in the pelvis to suggest it.

DR. FRANSEEN: That is why I have to explain it on the basis of tumor that distorts the capsule and extends along the medial side. It could be explained by a contiguous tumor. A tumor of adrenal origin is rare in the kidney. Clinically we usually call tumors of renal origin hypernephromas, hence, this could conceivably be either a tumor of adrenal origin or a carcinoma of the kidney, which could conceivably arise from a rest at this site in the kidney. My next choice is a lymphoma, which could give a lesion in both these locations.

#### CLINICAL DIAGNOSIS

Changes consistent with either lymphoma or Ewing's tumor

#### DR. FRANSEEN'S DIAGNOSIS

Metastatic tumor of adrenal or renal origin?  
Lymphoma?

#### ANATOMICAL DIAGNOSIS

Eosinophilic granuloma of bone.

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The surgeon who was in charge of this case did not commit himself to a diagnosis beyond saying that it was a bone tumor. I think he gambled on its being primary and discarded the long history of back symptoms, because instead of doing a biopsy he did a resection of the rib. The specimen which we received was unlike anything we had ever observed before. On microscopic examination it was evidently a granulomatous process with a good deal of fibrous tissue and with a great many foci of giant cells, which tended to be clumped in tuberculoid foci and an enormous number of eosinophils. The clumping of the giant cells and epithelioid like monocytes make one think of tuberculosis, but there was no caseation. It also made one think of syphilis, but eosinophils would be extraordinary in syphilis. It looked a good deal more like a sarcoid, although the tubercles were not well enough formed even for that diagnosis.

I should have been unable to make a diagnosis if I had not had the opportunity of seeing two manuscripts, one by Lichtenstein and Jaffe and one by Otani and Ehrlich as yet unpublished but shortly to appear in the *American Journal of Pathology* in which the authors independently describe several cases of this condition and agree to call it eosinophilic granuloma of bone. It is a histologically specific lesion which occurs generally in flat bones very frequently follows a history of trauma and apparently runs a perfectly benign course following resection or mild radiation. The histologic picture is so characteristic that I do not believe it could be mistaken for anything else. I am sure that is what we are dealing with here, and I suspect he is well so far as this condition is concerned but may continue to have "back trouble" for the rest of his life.

DR. WILLIAM B. BREED: Is Dr. Hampton still interested in the kidney?

DR. HAMPTON: I wonder if I made up my mind that the tumor in the rib was lymphoma and then used my imagination. I am convinced that a tumor in the rib such as this and associated with a retroperitoneal mass is usually lymphoma.

DR. F. DENNETTE ADAMS What about the nausea and fainting?

DR. MALLORY Nausea, vomiting, prostration and fainting are the ordinary symptoms of so-called "sacro-iliac disease", all of this would go with back strain.

A PHYSICIAN Have you any other cases in your files under this category?

DR. MALLORY I may have one, that of a child who was supposed to have had Schüller-Christian's disease and on whom a biopsy showed many giant cells and numerous eosinophils. Unfortunately the biopsy was from a lymph node, not from one of the bone lesions, so I am not certain about it.

Schäirer\* has, however, reported a case of a peculiar granulomatous lesion in a child's skull, with a marked reaction of eosinophils as well as of giant cells, which seems to have been essentially similar.

DR. GRANTLEY W. TAYLOR Have the other patients had eosinophilia?

DR. MALLORY I cannot remember. Apparently that was the only lead in this case.

DR. HAMPTON Do you have eosinophilia with coccidioidal granuloma?

DR. MALLORY I think not.

\*Schäirer E. Ueber eine eigenartige Erkrankung des kindlichen Schädels (Osteomyelitis mit eosinophiler Reaktion). *Zentralbl f allg Path u path Anat* 71:113-117, 1938.

# The New England Journal of Medicine

Formerly the  
Boston Medical and Surgical Journal

Established in 1829

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND  
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE  
ON PUBLICATIONS

Official Organ of

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MATERIAL for early publication should be received not later than noon on Saturday.

THE JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway Boston, Massachusetts.

## THE PRICE OF SECURITY

OCCURRENCES that have apparently never happened before, in the world's memory are now part of the daily news, we are living hour by hour on our regular shot of excitement, and miss it if it fails us, as the addict misses his morphine or his cocaine. Europe's catastrophe and the rise of a central hegemony keep the pulse quickened as the news symphonists play upon the changing strings of current events the Far East and the Near East and our Latin neighbors to the south furnish a fairly steady source of stimulation to the emotions, and a presidential campaign of a new pattern and intensity titillates the American temperament between its bouts of more distant agonizings.

It is a fair commentary on what we can take,

on how readily we can accustom ourselves to changes of ideas, at least if given only a reasonable time to do so. The months before Munich gave us as uneasy a feeling as we have experienced since our faith in the progress of the stock market onward and upward forever was shattered a decade ago. The spring military successes in Europe, and particularly the unorthodox, out-of-uniform infiltrations, filled the hearts of those Americans who live within a generous distance of an arsenal or a navy yard with an emotion closely akin to panic.

The long and the short of it is that we do not like modern totalitarian methods of doing things. Neutrality or no neutrality, we distrust and dislike bitterly those nations that employ such methods of achieving their ends. We may not be engaged in military conflict, but so long as we have reason to fear such nations, they are the enemy.

The erasure of neutral countries and the collapse of France have cleared the air. There is no longer any question as to whether the United States will become involved. Economically we are involved and the only way that we may possibly avoid being much more seriously, and perhaps disastrously involved is by preparing swiftly but intelligently, to defend ourselves against every type of attack. For this we must have courageous, far-sighted leadership, we must have an understanding of the problems to be met and the sacrifices to be made, we must have a logical program that we can understand and approve.

The medical profession, as usual, will carry its share of the burden. Comparatively few of us will be called on to serve in the armed forces of the country. For all, however, there will be extra work to do, mostly of an unpretentious nature. We can all signify to our own leaders, by executing promptly the questionnaire that has been sent to us, our willingness to do the job for which we are best suited. We can all work toward improving the morale and the confidence of the nation, and for this task our opportunities are unexcelled.



## FLUOROSCOPY AND EARLY TUBERCULOSIS

WHAT are physicians doing to raise their "batting average" in the very early diagnosis of tuberculosis? In 1935 the Council on Medical Education and Hospitals of the American Medical Association<sup>1</sup> showed that only 13 per cent of those admitted to sanatoriums in the country as a whole were in the minimal stage of tuberculosis, 30 per cent were in the moderately advanced stage, and 57 per cent in the far advanced stage. From the Metropolitan Life Insurance Company Sanatorium at Mount McGregor, New York, however, comes news<sup>2</sup> that 59 per cent of those admitted from 1930 to 1938 were in the minimal stage, 36 per cent of the cases were moderately advanced, and only 5 per cent far advanced. These figures are a reversal of those reported for the country at large.

These good results in early diagnosis apparently evolve from a systematic case-finding program among all employees of the Metropolitan Life Insurance Company. The first essentials of this program are the complete medical examination of all applicants and re-examination each year or oftener of those in the service of the company. But most important is the fact that fluoroscopic examination of the chest by trained experts has been made a part of each annual examination and is carried out following respiratory diseases and frequent colds. This case-finding technic deserves close scrutiny if it can improve the diagnosis of minimal tuberculosis so effectively. The second part of the program concerns adequate care of the early tuberculous lesion. Eighty per cent of the patients who exemplified both early detection and adequate treatment were at work or able to work five years after discharge. These results at Mount McGregor are impressive and demonstrate not only the necessity of early diagnosis but the need for early and adequate sanatorium care.

Fluoroscopic study, with x-ray confirmation, is important for the early detection of minimal tuber-

culous disease. But to this must be added the attempt to elicit a history of exposure, of hazardous occupation or of familial disease, together with a complete examination of the patient. Fluoroscopic examination may lead to a false sense of security for the physician not adequately trained in its use. But wisely and judiciously employed, as an adjunct to the usual complete medical examination, fluoroscopy should extend the physician's resources in the early diagnosis of tuberculosis and in the detection of conditions within the chest too small to give physical signs or too early to produce significant symptoms.

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- 1 Council on Medical Education and Hospitals of the American Medical Association. Survey of tuberculosis hospitals and sanatoriums in the United States. *J A M A* 105:1855-1915, 1935.
- 2 *Statistical Bulletin*. Metropolitan Life Insurance Company, September, 1939.

## MEDICAL EPONYM

### COHNHEIM'S AREAS

Julius Cohnheim (1839-1884), assistant in the Pathological Institute of Berlin, published an article entitled "Ueber den feineren Bau der quer gestreiften Muskelfaser [On the Microscopic Anatomy of Striated Muscle Fibers]" in *Virchow's Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* (34:606-626, 1865). A portion of the translation follows:

The frozen muscle can be cut with a chilled razor blade, and cross sections may be prepared with the greatest ease. If the cross section is spread in a 0.5 per cent sodium chloride solution, avoiding all pressure, it appears under the microscope as a varying number of unequally compressed round or elliptical, somewhat refractile disks, between which may be seen traces of a threadlike connective tissue. These disks, which are cross sections of individual muscle fibers, are enclosed and outlined by a definite, double circular or elliptical margin, obviously the visible expression of the sarcolemma. The surfaces of the disks enclosed by this outline are composed of two distinct substances, one quite transparent and glistening, and one less transparent and dull. The dull substance is arranged in mosaic form in the shape of innumerable small triangles, quadrangles and pentagons, which are separated from each other by the narrow seams of the transparent substance.

R.W.B.

## MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS  
AND GYNECOLOGY\*

RAYMOND S. TITUS, M.D., Secretary  
330 Dartmouth Street  
Boston

## FATAL DOUBLE PNEUMONIA IN PREGNANCY

Mrs. M.B., a thirty five year-old para II, entered the hospital on December 31, 1938 with a diagnosis of pneumonia. She was approximately at term.

The family history was non-essential. The patient's past history was unimportant. One previous pregnancy was terminated by a low forceps delivery. Catamenia began at eleven years regular with a twenty-eight-day cycle and lasted one and a half days. The last menstrual period began on April 8, and confinement was expected on January 15, 1939.

At the time of the first examination about July 1 the patient weighed 147 pounds. The blood pressure was 120 systolic, 70 diastolic. The heart was not enlarged, there were no murmurs. The lungs were clear and resonant, there were no rales. The abdomen was soft, no masses and no areas of tenderness were noted. The fundus was forward, the size of a three months pregnancy, and movable. On inspection the cervix showed a deep laceration on the left side.

The pregnancy progressed normally except for a very severe cold in November which left the patient with a persistent cough. On December 30 the weight was 166 pounds. The blood pressure was 124 systolic, 80 diastolic. The cough persisted. She had no temperature but was advised to go into the hospital for the purpose of getting rid of the infection and of awaiting labor. This she planned to do on January 1, 1939.

On December 31, however, the patient telephoned that she was feeling much worse, she was advised to go directly to the hospital. The temperature on admission was 101°F, the pulse 120, and the respirations 32. An internist was called in consultation. He found dullness over the right back from the region of the midscapula to the base, diminished breath sounds and fremitus in this area, and bronchovesicular breathing in the fourth left interspace at the edge of the sternum. His impression was that she had lobar pneumonia and he advised a blood culture, sputum typing

and, if the type proved treatable, serum. The white-cell count was 21,050. Type 3 pneumococci were found in the sputum. Type 3 serum was started immediately and 410,000 units were given during the next twenty four hours.

On January 1, labor began. This was normal and comparatively rapid, the baby, a girl weighing 7 pounds being delivered normally after a total labor of less than five hours. During labor 1½ gr of Nembutal was given as an analgesic. The patient was given no other anesthesia as she was in an oxygen tent. The baby survived.

The same evening, pneumonia developed in the left chest. The temperature was 102°F and the pulse 108 and of good quality. The next morning January 2, the patient was definitely worse. The white-cell count was 2300 and a blood transfusion was given. The patient went steadily downhill and died during the evening of January 3.

*Comment.* This case illustrates the extreme seriousness of pneumonia during pregnancy. The patient was treated as conservatively as possible from the beginning. Although not ill, hospitalization was advised for the purpose of rest and in the hope that the persistent respiratory infection might clear up. Pneumonia developed before this could be accomplished. Medical consultation, typing serum therapy, the use of an oxygen tent and constant nursing care accomplished nothing. As is so often true with sick pneumonia patients, labor was easy and apparently took nothing out of the patient. The small amount of Nembutal certainly could have done no harm although its use as an analgesic in the presence of respiratory infection is generally contraindicated. Spinal anesthesia would have been ideal had operative interference been necessary. It is not unduly optimistic to say that, today, chemotherapy might have saved this patient's life.

## MISCELLANY

## THE PHYSICALLY BELOW PAR CHILD

In the early years of this century the term "pretuberculous" was used to describe children who were in contact with an adult case of tuberculosis and those who were underweight or apparently below par in health. These children it was believed, were in need of an abundance of fresh air, rest and additional food. Special open-air classes were organized for them on the theory that by such devices the development of tuberculous might be prevented. As the years passed, the soundness of these ideas was challenged and recently a Committee on Care and Education of Below Par Children has re-investigated the subject. Extracts of the report (*The Physically Below Par Child* 20 pp. New York: National Tuberculosis Association 1940) of this committee follow.

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be published.

Many school departments make special provision for so-called "exceptional" children, including the visually handicapped, the hard of hearing, those with heart disease and those presumably in danger of developing tuberculosis. Various terms have been used to describe these children, such as delicate, undernourished, underweight, handicapped and lowered vitality. Because open air classes have been stimulated largely by tuberculosis associations throughout the country, the National Tuberculosis Association has felt a responsibility to review the problem and therefore appointed a committee to study the situation.

### *Changing Concepts*

In the early open air classes, emphasis was placed on malnutrition and anemia—either or both of which were considered at that time to be predisposing factors in the development of tuberculosis—and on known contacts with an open case of tuberculosis. Today it is recognized that no matter how pale or undernourished a child may be he will not develop tuberculosis unless he actually takes tubercle bacilli into his body. Therefore the term "pretuberculous" is no longer acceptable and its use should be discarded. The best way to prevent infection among children is to remove the case of tuberculosis from the home. Infection in a child can be detected by the tuberculin test. Tuberculous disease in children between the ages of five and fifteen years is relatively unimportant, the tubercle bacilli are apparently walled off and cause little damage. The walling-off process seems to operate just as rapidly and completely if the child remains in school and participates in the normal activities of child life as when strict bedrest is instituted. A school child who has a positive tuberculin reaction but whose x-ray reveals nothing abnormal, who is apparently in good health, and who after a thorough investigation of his associates at home and elsewhere is found not to be in contact with an open case of tuberculosis, usually does not need special care. Nor is such a child capable of transmitting tuberculosis. He is, however, entitled to the health supervision which is due every child. Throughout adolescence and early adult life he should be given an x-ray examination annually and watched.

There remains a group of tuberculous children for whom special care is necessary. These children may have such extensive infection that the body cannot well control it, or clinically serious tuberculous disease may have begun. Such children, both for their own welfare and also to protect others from the disease, need special care. The question arises whether it is not better to arrange home or institutional care for this group. Their number in any one locality is usually so small that either the expense of a special teacher for them or the transportation costs of collecting daily in one place a sufficient number to warrant a full time teacher, is economically impractical. It is believed that such convalescent care as is needed must be worked out in the light of available local resources.

### *Below Par Children*

"Malnutrition" is a loosely used term. Underweight is not necessarily a symptom of malnutrition, nor are all undernourished children underweight. The judgment of the physician based on one routine physical examination is not always dependable, for studies have shown that competent physicians vary widely in their independent judgments of nutritional status in the same children. Nutrition is not a single entity due to a single cause. Vitamin status, the chemical constituents of the blood, and types and degrees of anemia are all recognized as important indices of nutritional status.

However, the physician can with some degree of reliability select those children who are physically below par. They include those who exhibit such symptoms as lack of stamina, lassitude, failure to gain weight, and so forth. Only a comparatively small number are below par primarily because of a condition needing medical care. For those who do need medical care the course of action should be to set the machinery going to obtain adequate medical care.

A second group are those who are temporarily below par following illnesses or operations. Often such a child is better off in the ordered ways of school life although he is not able to carry a full program of work and activity.

In the great majority of below-par children the cause is usually determinable only after study of the child in relation to his home and family. Poverty, ignorance and maladjustment may be factors. Only after a careful study of such factors can one hope to solve the problem.

### *Are Special Classes Necessary?*

Special classes for "exceptional" children have undoubtedly made a contribution to the improved health of school children. One type, the open air class, has emphasized fresh air, food and rest. Fresh air has mistakenly been interpreted as meaning large volumes of outdoor air regardless of temperature. But recent studies have shown that cool air in gentle motion provides the best condition for comfort and for health. Supplementary feeding at school is open to question. Adequate food and regular meals at home are best, and supplementary feeding if indicated, must follow the needs of the individual case. Whatever the cause of inadequate food may be, the solution lies not in special classes but in home adjustments. Rest is an important need for the below-par child. Open air classes have demonstrated the value of periods of rest. The amount and the duration of the additional rest requirement for the individual child should be based on medical opinion.

### *Special Care*

Against this background of change in theories and facts the present-day problem of how to care for the below-par child must be met. Groups including the deaf, the crippled, those with heart disease and the visually handicapped need special adjustment of school procedures. For children with clinical tuberculosis special provision must be made for they are sick children. There remains a sizable but less well-defined group which includes children below par because of a condition needing medical care, or, temporarily, following an illness or operation, or from a variety of causes which may be socioeconomic and related to the home. The school should provide for these below-par children a lightened school program together with extra rest. The easiest way to do this is by means of the segregated special class, but it is costly and educationally and socially unsatisfactory. How can the school best meet its problem?

The school physician can, in the course of school physical examinations, select the below-par group for intensive study. The school physician, nurse and teacher can, by follow-up study of the child, the parents and the home, gain a better understanding of the underlying causes of the condition. These causes can, to a large extent, be removed or mitigated by making social and economic adjustments in the home.

In summary, the responsibility of the care of the below-par child should be divided between the home and the school. Segregation in special classes is not necessary and is detrimental to the child's education and social development. Supplementary feeding at school is open to ques-

non. School procedures should be adopted for individual children to provide for rest periods, a lightened school program with avoidance of undue strain and attendance at regular classes for as much of the academic program as the child is able to carry. This program formulated for elementary school children should also be extended to junior and senior high-school students.—Reprinted from *Tuberculosis Abstracts* (July, 1940)

## RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JUNE 1940

DISEASE	JUNE 1940	JUNE 1939	FIVE YEAR AVERAGE
Anterior poliomyelitis	2	3	4
Chicken pox	851	854	1119
Diphtheria	9	7	16
Dog bite	1292	1587	1398
Dysentery bacillary	11	1	10
German measles	64	75	1378
Gonorrhea	292	415	431
Lobar pneumonia	227	236	278
Measles	5227	3918	2805
Meningococcus meningitis	1	5	6
Mumps	641	501	696
Paratyphoid B fever	6	7	12
Scarlet fever	381	439	60
Syphilis	389	417	436
Tuberculosis, pulmonary	103	275	304
Tuberculosis, other forms	25	36	38
Typhoid fever	7	9	7
Undulant fever	3	4	3
Whooping cough	578	551	555

Based on figures for preceding five years.

### RARE DISEASES

Anterior poliomyelitis was reported from Chicopee, 1  
Worcester 1 total, 2  
Anthrax was reported from Lynn 1 total 1  
Diphtheria was reported from Boston 1 Framingham  
2 Methuen 1 Sandwich 2 Worcester 3 total 9  
Dysentery bacillary was reported from Boston 1 Bur-  
lington, 5 Dedham, 1 Somerville, 1 Swampscott, 1  
Tewksbury 1 Woburn 1 total 11  
Infectious encephalitis was reported from Brockton 1  
Greenfield, 1 Salem 1 total, 3  
Meningococcus meningitis was reported from Boston 1  
total, 1  
Paratyphoid B fever was reported from Cambridge, 1  
Fall River 1 Marblehead 1 Marion 1 Somerville, 1  
West Boylston, 1 total 6  
Septic sore throat was reported from Boston, 4 Cam-  
bridge, 2 Danvers 6 Westboro, 1 total, 13  
Tetanus was reported from Burlington 1 West Stock-  
bridge, 1 total, 2  
Trichinosis was reported from Melrose, 1 Montague, 3  
Quincy 3 Wellesley 5 total 12  
Typhoid fever was reported from Boston 1 Brockton,  
1 Marlboro 1 Mattapoisett 1 Somerville 1 Weymouth  
2 total 7  
Undulant fever was reported from Auburn 1 Hope-  
dale 1 North Adams, 1 total 3

Pulmonary tuberculosis was reported at a record low  
figure both for this and any other month  
Measles and whooping cough were reported above the  
five year average.  
Meningococcus meningitis was reported at a record low  
figure, with the exception of that for 1933 which was  
equaled.  
Tuberculosis (other forms) showed record low inci-  
dence.

Bacillary dysentery, lobar pneumonia mumps and undu-  
lant fever were reported at expected levels.

Anterior poliomyelitis chicken pox, diphtheria and Ger-  
man measles were reported below the five year average.

Dog bite showed expected high seasonal incidence.

Animal rabies was reported at a low figure. Active foci  
were reported in Canton, Medway and Norwell.

## MAINE NEWS

### NEW OFFICERS OF MAINE MEDICAL ASSOCIATION

Dr P. L. B. Ebbett, of Houlton Maine, was elected  
president-elect of the Maine Medical Association at the  
annual meeting held at Rangeley Lakes on June 23 24  
and 25

The following standing committees were appointed

### SCIENTIFIC COMMITTEE

H. C. Scribner Bangor chairman  
C. C. Weymouth Farmington  
E. E. O'Donnell Portland  
L. H. Smith Winterport

### MEDICAL ADVISORY COMMITTEE

C. M. Robinson Portland, chairman  
Allan Woodcock, Bangor  
S. A. Cobb Sanford  
W. H. Bunker Calais  
C. H. Jamieson, Rockland  
F. H. Jackson Houlton  
F. B. Ames, Bangor  
The Secretary ex-officio

### COMMITTEE ON MEDICAL EDUCATION AND HOSPITALS

A. P. Leighton Portland, chairman  
C. D. North Rockland

### PUBLIC RELATIONS COMMITTEE

W. E. Kershner Bath chairman  
F. T. Hill Waterville  
H. C. Knowlton, Bangor  
C. W. Kinghorn, Kittery  
W. A. Ellingwood Rockland

### COMMITTEE ON SOCIAL HYGIENE

B. B. Foster Portland chairman  
B. S. Merrill Bangor  
C. B. Popplestone, Rockland

### CANCER COMMITTEE

Mortimer Warren Portland chairman  
Magnus Ridlon Bangor  
E. H. Rusley Waterville  
William Holt, Portland  
Bertrand Beliveau Lewiston

### PUBLICITY COMMITTEE

T. A. Foster Portland chairman  
The Secretary ex-officio

## NOTE

At the annual meeting of the Massachusetts Board of  
Registration in Medicine in July Dr Francis R. Mahony  
of Lowell and Dr Stephen Rushmore, of Boston were  
respectively elected chairman and secretary for the en-  
suing year

## CORRESPONDENCE

PHYSICIANS NEEDED  
FOR ARMY SERVICE

*To the Editor* With the likelihood of an augmented U S Army existing for a prolonged period, the War Department has been able to plan accordingly in considering medical personnel requirements

In reference to extended active duty for officers of the Medical Corps Reserve, important changes have been made. Reserve officers may now serve in Hawaii, Panama and other United States possessions, and may receive yearly extensions of active duty for an indefinite number of years until the international situation clarifies and until the future can be viewed with more certainty

Attached is a statement pertaining to extended active duty for physicians, which probably will be of interest to your readers

JAMES E. BAYLIS,  
Colonel, Medical Corps, U S Army,  
Executive Officer

War Department,  
Office of the Surgeon General,  
Washington, D C

\* \* \*

The physician, like every other American, has become actively interested in our national security and stands ready to contribute his services as required for military preparedness

The immediate problem in this connection is one that concerns the War Department and, primarily, the young physician. The War Department must procure sufficient additional personnel from the medical profession to augment the medical services of the Regular Army as the various increases are made in the strength of the Regular Army is authorized by Congress to meet the partial emergency. The young physician is especially concerned because for him to serve with the Regular Army is usually advantageous, and is often convenient.

Present plans of the War Department are designed to make service attractive and instructive for the young physician. If the physician holds a Medical Corps Reserve commission he can be ordered to active duty if he so requests. If he does not hold a commission, but is under thirty five years of age and is a comparatively recent graduate of an accredited school, he may secure an appointment in the Medical Corps Reserve for the purpose of obtaining extended active duty for a period of one year or longer. Duty is given at general hospitals and station hospitals and with tactical units, and embraces all fields of general and specialized medicine and surgery. Excellent postgraduate training is obtainable in connection with aviation medicine. After serving six months of active duty in the continental United States, a reserve officer may request duty in Hawaii, Panama or other United States territories and possessions. The initial period for duty is for one year, and yearly extensions are obtainable thereafter until the international situation becomes more clarified and the domestic military program becomes stabilized.

Many young doctors who have served with the Regular Army on extended active duty have taken the competitive examination for entrance into the Medical Corps of the Regular Army. Extended active duty affords an excellent opportunity for the physician to observe modern military medicine and the facilities that exist for a complete and comprehensive medical practice.

Pay is according to rank, and, including subsistence and quarters allowances for an officer with dependents, amounts to an annual sum of \$3905 for a captain and \$3152 for a first lieutenant, or, without dependents, to an annual sum of \$3450 for a captain and \$2696 for a first lieutenant. In addition, reimbursement is made for travel to duty station and return.

Further information may be obtained by writing to The Surgeon General, U S Army, Washington, D C.

## LICENSE REVOKED

*To the Editor* The license of Dr. Anthony Peter Carogana, 672 Broadway, Chelsea, was revoked by the Board of Registration in Medicine on July 11 because of conviction in court of abortion.

STEPHEN RUSHMORE, M.D., Secretary,  
Board of Registration in Medicine.

State House,  
Boston

INTERNS LICENSE LIMITED  
TO THREE YEARS

*To the Editor* I am enclosing for your information a copy of the text of a circular letter which has been sent to the superintendents of all the hospitals in the State.

STEPHEN RUSHMORE, M.D., Secretary,  
Board of Registration in Medicine.

State House,  
Boston

\* \* \*

This is to inform you that at the meeting of the Board of Registration in Medicine held June 27, 1940, it was

**VOTED** To limit the period for which an intern's license is to be issued to three years

It is the opinion of the Board that if a physician wishes to practice in Massachusetts for more than three years he should be registered as a qualified physician, which requires an examination.

As applications are made to the Board the applicants will be informed as to the change of ruling, but you are requested to bring this matter to the attention of the interns and residents now in your institution. The new ruling does not affect licenses already issued, but will apply to new licenses and to extensions.

## REPORTS OF MEETINGS

## HARVARD MEDICAL SOCIETY

A regular meeting of the Harvard Medical Society was held at the Peter Bent Brigham Hospital on March 26, with Dr. Soma Weiss presiding.

The first case presented was that of a thirty five year-old man who entered the hospital three weeks before, with a one day story of crampy abdominal pain unrelieved by soda or attempts at vomiting, and culminating in an episode of excruciating epigastric pain and incipient shock. For two years the patient had been known to have chronic ulcerative colitis, for which he had been admitted to the medical wards on three occasions, the last time two weeks before the present admission. He had been feeling well during the interim. On physical examination the chief findings were extreme pallor and the abdominal signs. There was marked spasm of the abdominal muscles, accompanied by tenderness only in the upper quadrants, and reflex tenderness referred to a point just above the umbilicus. The temperature was 100.2°F, the pulse 82, and the

respirations 24. The white-cell count was 21,000 and the red-cell count 3,800,000. The urinary diastase was positive in a dilution of 1:234. Treatment consisted of watchful waiting together with Wangenstein drainage, high Fowler's position and parenteral fluids. Gradual improvement occurred and all signs and symptoms had disappeared after fifteen days.

Dr Joseph A. Capps stated that in Chicago such a complex would be suspected of being due in anebic dysentery with or without liver involvement, in view of their recent experience with bizarre cases. Diarrhea and even cramps may be lacking and yet the patient turn out to have amebiasis with hepatitis or liver abscess. Dr Joseph H. Pratt cited the elevated pulse and temperature as well as the tender abdomen on the first day as being distinctly against pancreatitis. He stressed the value of a diastase curve rather than a single determination in questionable cases of pancreatitis and advocated the use of urinary rather than blood diastase tests. He added in reply to a question that pancreatitis secondary to perforation of an abdominal viscus may give an elevated diastase level. Dr Weiss emphasized the importance of conservative treatment in most cases of acute pancreatitis, unless there are surgical complications.

The medical case was that of a thirty-two-year-old man who entered the hospital with a one-day history of dyspnea, pain in the right chest and hemoptysis. At the age of seven years there had been chorea and there was an attack of acute rheumatic fever four years later. At thirteen he was refused life insurance on the basis of "heart disease." His first hospital admission was at twenty-one, when he complained of dyspnea, cough and pain in the right chest. At that time physical examination revealed enlargement of the heart to the right and left, marked systolic and diastolic murmurs and a thrill at the apex. In the following eleven years there were ten admissions, nine of them for the same symptoms and with the same physical findings as originally. The last episode, six months previously was complicated by a left hemiplegia and a questionable pulmonary infarct. Physical findings on the present admission were unchanged in regard to the heart, but there were, in addition, dullness and basal rales in the right axilla.

Dr Capps considered the presence of hemoptysis and the localization of the pleural pain very suggestive of lung infarct. Dr Paul D. White said that the roentgenograms indicated a tricuspid-valve lesion despite the lack of physical findings. He suggested that a deep neck pulsation might be felt in the absence of superficial pulsation and distention. Dr Weiss believed that the lack of these findings and the absence of a tricuspid murmur ruled out this lesion. Dr Samuel A. Levine stated that the diagnosis in such a case is difficult; he suggested that it is only when there is a sustained elevation of venous pressure after the patient's condition has improved that one is justified in using that means of diagnosing tricuspid stenosis. He reminded the audience of the advantage of such a lesion in mitral stenosis, in which case the prognosis is improved over that of the uncomplicated case.

The speaker of the evening was Dr Joseph A. Capps, of Chicago, whose subject was "The Prognosis in Bacterial Endocarditis." It was the surprising recovery of one of his office patients in 1910 that stimulated Dr Capps to investigate the outcome of subacute bacterial endocarditis particularly in office and outpatient clinics where less severe cases are found. Postmortem evidence of healed bacterial endocarditis was reported as early as 1900 and the stages of active bacterial growth, vegetations without bacteria and complete healing were recognized.

diagnosed due to the difficulty of establishing adequate criteria for diagnosis. Positive blood cultures alone are not necessarily significant, for they may be present in cases of tonsillitis, sinusitis and otitis media due to *Streptococcus viridans*. Also, transient murmurs may accompany hemorrhage or fever. Therefore, the speaker suggested as necessary criteria the presence of the characteristic evanescent murmurs, a consistent temperature, a focus of infection and a positive blood culture. Embolic phenomena may or may not be present.

A study of the rare reports of clinical recoveries indicated that there were epidemics during which the majority of recovered cases occurred, probably due to less severe infection. Furthermore, comparison of the incidence of subacute bacterial endocarditis from various clinics revealed a definite peak in 1921 to 1924 with a general decrease since then. It was during that short period that the majority of recoveries took place, and Dr Capps has had none since 1924. He suggested the use of the term arrest rather than recovery.

Of 139 cases which he has observed, Dr Capps had 10 patients who survived for one to two years and then died of recurrence or of cardiac failure. There are 11 patients who lived from eight to nineteen years from the onset. An investigation of the findings in the recovered as contrasted with the fatal cases revealed the milder characteristics of the former (Table I).

TABLE I Findings in Recovered and Fatal Cases of Bacterial Endocarditis

Findings	Recovered Cases	Fatal Cases
Rheumatic fever	54%	58%
Temper	99 to 101 F	101 to 105 F
Splenomegaly	33%	75%
Hematuria and hemoglobinuria	65%	75%
Prothrombin	25%	80%
Cerebral embolus	—	20%
Osteal nodes	—	8%

In regard to treatment, Dr Capps stated that nothing is specific; he has used sodium cacodylate in all his cases. Although the use of sulfanilamide and its related compounds with or without heparin appears promising, the speaker predicted that longer follow-ups may prove the enthusiasm premature. He concluded that enforced and prolonged bedrest in mild cases may lead to cure. He reminded the group in closing that recovery does not necessarily rule out the possibility of the patients having had subacute bacterial endocarditis.

Dr White reported the only recovery known in Boston hospitals, wherein a patient lived five years before dying of a new attack, with old healed lesions being proved at autopsy. A recent case in which the patient died of acute rheumatic fever was shown at autopsy to have a recently healed bacterial endocarditis. The latter patient was treated with heparin and sulfanilamide, a method that has shown encouraging results during the past two years. There has been one other case apparently arrested out of 26 thus treated. On the whole, the drugs are considered definitely beneficial since life seems to be prolonged and the patient made more comfortable.

Dr Samuel A. Levine suggested that the lack of reported cures in Boston may be attributed to skepticism toward the diagnosis for he recalled a case which in retrospect was characteristic but otherwise diagnosed since the patient recovered. Cases with obscure sustained fevers or acute rheumatic fever may well include some of bacterial endocarditis, he stated particularly since bacteriological methods at best are only 70 to 80 per cent positive in those cases in which at autopsy *Streptococcus viridans* is recovered.

## NOTICES

## ANNOUNCEMENT

RALPH VOLK, MD, announces the removal of his office from 311 Commonwealth Avenue, Boston, to 375 Commonwealth Avenue, Boston

### CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	ORTHOPEDIC CONSULTANT
Lowell	August 2	Albert H. Brewster

No other clinics will be held during the month of August

## SOCIETY MEETINGS AND CONFERENCES

- SEPTEMBER 2-6 — American Congress of Physical Therapy Page 862 issue of May 16
- OCTOBER 6-11 — Annual meeting of the American Academy of Ophthalmology and Otolaryngology Page 81 issue of July 11
- OCTOBER 8-11 — American Public Health Association Page 655 issue of April 11
- OCTOBER 11, 12 — Pan American Congress of Ophthalmology Page 898 issue of May 23
- OCTOBER 14-25 — 1940 Graduate Fortnight of the New York Academy of Medicine Page 938 issue of May 30
- OCTOBER 21 — American Board of Internal Medicine Page 369 issue of February 29
- JANUARY 4, 1941 — American Board of Obstetrics and Gynecology Page 1064 issue of June 20
- APRIL 21-25, 1941 — American College of Physicians Page 1065 issue of June 20

## DISTRICT MEDICAL SOCIETY

## MIDDLESEX NORTH

JULY 31

OCTOBER 30

## BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

*Modern Dermatology and Syphilology* By S. William Becker, MD, associate professor of dermatology and syphilology, Kuppenheimer Foundation, University of Chicago, and Maximilian E. Obermayer, MD, assistant professor of dermatology and syphilology, Kuppenheimer Foundation, University of Chicago. 4°, cloth, with 461 illustrations and 32 colored plates. Philadelphia: J. B. Lippincott Company, 1940. \$12.00.

*Psychology and Psychotherapy* By William Brown, D.M. (Oxon), D.Sc. (Lond.), F.R.C.P., Wilde Reader in Mental Philosophy and director of the Institute of Experimental Psychology, University of Oxford, etc. Fourth edition. 8°, cloth, 260 pp. Baltimore: Williams & Wilkins Company, 1940. \$4.75.

*The Surgery of the Alimentary Tract* By Sir Hugh Devine, M.S., F.R.A.C.S., F.A.C.S., formerly senior sur-

geon, St. Vincent's Hospital Clinical School, Melbourne, Stewart Lecturer in Surgery, Melbourne University, etc. 8°, cloth, with 690 illustrations, some in color. Baltimore: Williams & Wilkins Company, 1940. \$15.00.

*The Public Health Nurse and Her Patient* By Ruth Gilbert, supervisor of social work, Psychiatric Service in the Community, New Haven, Connecticut, formerly mental health supervisor, Visiting Nurse Association, Hartford, Connecticut. 8°, cloth, 396 pp. New York: Commonwealth Fund, 1940. \$2.25.

*A Method of Anatomy, Descriptive and Deductive* By J. C. Boileau Grant, M.C., M.B., Ch.B., F.R.C.S. (Edin.), professor of anatomy, University of Toronto. Second edition. 4°, cloth, 794 pp., with 651 illustrations. Baltimore: Williams & Wilkins Company, 1940. \$6.00.

*A Handbook for Dissectors* By J. C. Boileau Grant, professor of anatomy, University of Toronto, and H. A. Cates, associate professor of anatomy, University of Toronto. (A companion volume to *A Method of Anatomy*). 12°, cloth, 239 pp., with 3 illustrations. Baltimore: Williams & Wilkins Company, 1940. \$2.50.

*Cancer: A manual for practitioners* The Committee on Publications. George W. Holmes, M.D., chairman, Shields Warren, M.D., and Ernest M. Daland, M.D. Edited by Channing C. Simmons, M.D. 8°, cloth, 284 pp. Boston: Rumford Press, 1940. \$2.00.

*A Textbook on Physiology* By William H. Howell, Ph.D., M.D., Sc.D., LL.D., emeritus professor of physiology, Johns Hopkins University, Baltimore. Fourteenth edition, thoroughly revised. 8°, cloth, 1117 pp., with 330 illustrations. Philadelphia and London: W. B. Saunders Company, 1940. \$7.50.

*Medical Nursing* By Edgar Hull, M.D., F.A.C.P., clinical professor of medicine, Louisiana State University School of Medicine, visiting physician, Charity Hospital of Louisiana, New Orleans, Christine Wright, R.N., B.S., instructor of nursing arts, Charity Hospital School of Nursing, New Orleans, etc., and Ann B. Eyl, B.S., assistant dietitian, Cook County School of Nursing, Chicago, formerly instructor in Home Economics, University of Kentucky, Lexington, etc. 8°, cloth, with 168 illustrations, including 11 color plates. Philadelphia: F. A. Davis Company, 1940. \$3.50.

*Medical Diseases of War* By Sir Arthur Hurst, M.A., D.M. (Oxon), F.R.C.P., lieutenant-colonel, late R.A.M.C., consulting physician to Guy's Hospital, etc., with the co-operation of H. W. Barber, M.A., M.B. (Cantab.), F.R.C.P., physician in charge of the Skin Department, Guy's Hospital, F. A. Knott, M.D. (Lond.), M.R.C.P., bacteriologist to Guy's Hospital, and T. A. Ross, M.D. (Edin.), F.R.C.P., late medical director of Cassel Hospital for Functional Nervous Disorders. 8°, cloth, 327 pp., with 37 illustrations and 4 plates. Baltimore: Williams & Wilkins Company, 1940. \$5.50.

*The Chemistry of Natural Immunity* By William Frederick Koch, Ph.D., M.D. 8°, cloth, 199 pp., with 40 illustrations. Boston: Christopher Publishing House, 1938. \$2.00.

*A Man Who Found a Country* By Dr. A. Nakashian. 8°, cloth, 279 pp. New York: Thomas Y. Crowell Company, 1940. \$2.75.

*The Head and Neck in Roentgen Diagnosis* By Henry K. Pancoast, M.D., late professor of radiology and director of the Department of Radiology, University of Pennsylvania, Eugene P. Pendergrass, M.D., professor of radiology and director of the Department of Radiology, University of Pennsylvania, and J. Parsons Schaeffer, M.D., Ph.D.,

professor of anatomy and director of the Daniel Baugh Institute of Anatomy, Jefferson Medical College. 4 cloth, with 1251 illustrations. Springfield, Illinois: Charles C Thomas, 1940 \$12.50

*It Is Your Life. Keep healthy stay young live long.* By Max M Rosenberg M.D. 8 cloth 450 pp. New York: Scholastic Book Press. \$2.50

*Simplified Diabetic Manual with 163 International Recipes (American Jewish French German Italian Armenian etc)* By Abraham Rudy M.D., associate physician and chief of the Diabetic Clinic, Beth Israel Hospital, Boston, instructor in medicine Tufts College Medical School etc. Introduction by Dr Frederick M Allen. 8 216 pp., with 14 tables, and 18 illustrations. New York: M Barrows & Company Inc. \$2.00

*Endocrine Therapy in General Practice* By Elmer L. Sevringhaus, M.D., F.A.C.P., professor of medicine, University of Wisconsin Madison Wisconsin editor Department of Endocrinology *The Year Book of Neurology Psychiatry and Endocrinology*, 8 cloth 239 pp., with 49 illustrations. Chicago: Year Book Publishers, Inc. \$2.75

*Dermatologic Therapy in General Practice* By Marion B. Sulzberger, M.D., assistant clinical professor of dermatology and syphilology Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital of Columbia University associate attending dermatologist, Montefiore Hospital New York City and Jack Wolf M.D. attending dermatologist and syphilologist, Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital of Columbia University director of dermatology New York City Cancer Institute. 8 cloth 680 pp., with 65 illustrations and 25 tables. Chicago: Year Book Publishers, Inc. \$4.50

*Greens Manual of Pathology* Revised and enlarged by H. W. C. Vines M.A., M.D., director of the Charing Cross Hospital Institute of Pathology. Sixteenth edition. 8 cloth with 701 illustrations. Baltimore: Williams & Wilkins Company 1940 \$8.50

*Clinical Diabetes Mellitus and Hyperinsulinism* By Russell M. Wilder M.D., Ph.D., F.A.C.P., professor and chief of the department of medicine, The Mayo Foundation for Medical Education and Research, University of Minnesota head of the Section on Metabolism Therapy Division of Medicine, The Mayo Clinic, Rochester Minnesota. 8 cloth 459 pp., with 19 illustrations. Philadelphia and London: W B Saunders Company 1940 \$6.00

## BOOK REVIEWS

*Mineral Metabolism* Alfred T. Shohl M.D. 8 cloth 384 pp., with 41 tables. New York: Reinhold Publishing Corp. 1939 \$5.00

This valuable book is one of the series of scientific and technologic monographs published as part of a joint project of the American Chemical Society and the National Research Council. The editors include such eminent figures as W. A. Noyes and W. Mansfield Clark; they are responsible for the selection of timely subjects and of authors who are recognized as authorities in their respective fields. They have also reviewed critically the manuscripts submitted. The co-operative effort thus represented in this monograph has succeeded admirably.

The subject of mineral metabolism is of increasing im-

portance due to recent advances in the physiology of acid-base balance and of water metabolism, to the newly established roles of sodium and potassium in adrenal insufficiency and to the recent interest in traces or small quantities of certain essential minerals corresponding to the small but essential amounts encountered among the vitamins. The author, a research associate in pediatrics at Harvard University for more than ten years, worked in the fields of acid-base equilibrium and mineral metabolism. He has also had considerable clinical experience, having been associate professor of pediatrics at Western Reserve University from 1928 to 1933.

The book is compact enough to be read in its entirety yet, with its well-chosen bibliography by chapters, it will serve as a reference guide for detailed study. There is a brief introductory chapter concerned with general orientation and a concise list of definitions of terms. Those who do not yet feel quite at home among "milliequivalents" and "osmols" will be grateful for its inclusion. There follows a simple description of the mineral composition of the body and its components and organs and of the various secretions, excretions and internal secretions. The roles of certain ionic groups and elements, such as total base, chloride, bicarbonate, calcium and magnesium, phosphorus, sulfur, iron and iodine, are summarized and those minerals found in small but often essential traces are reviewed. The main emphasis of the concluding chapters, however, is on physiologic functions, and this discloses the complex relations of several elements under each function. Water metabolism, acid-base equilibrium, growth, pregnancy and lactation are some of the functions thus discussed.

This monograph will be of great interest to the general medical reader as well as to the student of biochemistry and nutrition.

*Twilight of Man* By Earnest Albert Hooton. 8 cloth 308 pp., with 17 illustrations. New York: G. P. Putnam's Sons, 1939. \$3.00

The author's scholarship and literary skill make this book attractive to all readers, lay and professional. The title suggests both optimum and pessimism with respect to man. The reader will not be disappointed despite the writer's incisive criticisms. The first chapter discusses "The Simian Bases of Human Mechanics or Ape to Engineer." In the second chapter "The Lantern of Diogenes" is raised in the hope of arresting the course of man's degeneration. "The Making and Mixing of Human Races" is set forth in the next four chapters. The seventh chapter concerns itself with "Change and Decay in Americans: A plain talk to college students." The next deals with "Noses, Knowledge, Nostalgia: The marks of a chosen people." Then follows a chapter on "The Anthropological Prospect of the Survival of Human Liberty." The tenth and final chapter considers "The Wages of Biological Sin." One may say with certainty that many pleasant, instructive hours await those who have not yet read this Shavian-like book.

*The Essentials of Medical Treatment* By David Murray Lyon M.D., D.Sc., F.R.C.P. (Edin.). 8 cloth 448 pp., with 19 illustrations. Edinburgh: Oliver & Boyd 1939 15s.

This book comes from English sources, the author being professor of clinical medicine at the University of Edinburgh. He has covered his subject thoroughly and the book should be of value to the general practitioner of



Great Britain. All the drugs are listed in the dosages and form given by the British *Pharmacopoeia* and *National Formulary*, which do not in many cases conform to the standards in use in the United States. References are made, moreover, to local English spas and similar places of treatment. It is possible that a few American physicians could use this book to advantage.

*Proctoscopic Examination and Diagnosis and Treatment of Diarrheas*. By M. H. Strecher, M.S., M.D. 8°, cloth, 149 pp., with 39 illustrations. Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1940. \$3.00.

This book presents a brief outline of proctology, the diagnosis and treatment of diarrheas and the technic of proctoscopy. It is divided in two sections. The first deals with the technic of proctoscopy, presents a tabulation of 7406 proctoscopic examinations and gives a brief summary of the findings in each of the common anorectal diseases. The second section deals with the classification of diarrheas and briefly presents their main diagnostic and therapeutic features.

The author makes an earnest plea throughout the book for the use of the proctoscope as a diagnostic aid in a wide variety of conditions, both local and systemic. His classification of diarrheas is very comprehensive, although only a brief outline of the diagnosis and treatment of each type is given.

There are several simple drawings and photographs illustrating the gross pathologic anatomy of the common diseases of the rectum and colon.

*Principles and Practice of Aviation Medicine*. By Harry G. Armstrong, B.S., M.D. 8°, cloth, 496 pp., with 86 illustrations. Baltimore: Williams & Wilkins Co., 1939. \$6.50.

With the rapid growth of aviation, it is not surprising that a book on the subject of aviation medicine should appear. Dr. Armstrong, a member of the Medical Corps of the U. S. Army and director of the Aero Medical Research Laboratory, has written a book primarily intended as a textbook for students and as a reference work for those actively engaged in the practice of aviation medicine. The volume consists of twenty-seven chapters covering practically every aspect of this interesting subject, it is accurately compiled, with excellent illustrations, references to the literature and an index.

This book can be highly recommended for a selected group of physicians. There is an interesting introductory chapter on the history of aviation in relation to medicine, particular emphasis, naturally, being put on the development of the specialty in America. Considering the size of the book and the comparatively few illustrations, the price seems unnecessarily high.

*Population, Race and Eugenics*. By Morris Siegel, M.D. 12°, cloth, 206 pp. Hamilton, Ontario: Published by the author, 1939. \$3.00.

The author considers the aims of eugenics to be the discovery of those negative factors that will ultimately lead to a considerable reduction in the incidence and frequency of congenital degenerations and hereditary mental disorders and the further search of the positive factors that lead to a negative correlation between fertility and cultural and intellectual attainment. The first part of the

book is titled "Positive Eugenics" and is considered under the chapter headings of "Population and Eugenics," "Etology," "Constructive Recommendations," "Racial Theories in Relation to Eugenics" and "Rational Marriage." The second part, which is titled "Restrictive Eugenics," discussed under the chapter headings of "The Feeble-minded," "Mental Disorders," "Epilepsy," "Restrictive Measures" and "General Conclusions."

The author has carefully thought out his approach and has written in a style that will easily engage the interest of the average general reader, as well as that of those who professionally deal with this subject matter.

*Manual of Public Health Nursing*. Prepared by the National Organization for Public Health Nursing (Member of the National Health Council). Third edition. 12°, cloth, 529 pp. New York: Macmillan Co., 1939. \$2.50.

This manual has been entirely rewritten, and much new material has been added. Its purpose is to suggest procedures to serve as a guide to the public health nurse in the field. Parts I and II are devoted to the discussion of problems of administration and organization and of family-health service. Part III, comprising three-fifths of the volume, goes into the details of actual nursing procedure with respect to maternity cases, child health, school children, industrial cases, tuberculosis, genitoinfectious diseases and orthopedic cases. An appendix prescribes minimal qualifications for those appointed to positions in public-health nursing. The book is eminently practical and is to be commended for its strictly professional and businesslike presentation of factual information. One can find remarkably little to disagree with in the entire volume.

*Beyond the Clinical Frontiers: A psychiatrist views crowd behavior*. By Edward A. Strecker, A.M., Sc.D., Litt.D., M.D. 8°, cloth, 210 pp. New York: W. W. Norton & Co., 1940. \$2.00.

Dr. Strecker, the distinguished professor of psychiatry at the University of Pennsylvania, has had published in book form his series of Salmon Lectures, given at the New York Academy of Medicine, in which he summarizes some of the modern advances in psychiatry, particularly in relation to mental hygiene and planning for the future. The book is well written and adequately covers the field. There is an excellent bibliography. As a summary of modern psychiatry in relation to the world in general, this book is highly recommended.

*Handbook of Skin Diseases*. By Leon Hugh Warren, B.A., M.D., M.Sc. (Med.), with a foreword by Frederick D. Weidman, M.D. 12°, cloth, 321 pp. New York and London: Paul B. Hoeber, Inc., 1940. \$3.50.

This manual is intended to supply a much needed volume in dermatological literature, namely a "memory aid" and a reference guide of some two hundred and fifty skin diseases. In both these concepts it serves the purpose, both for the general practitioner and the teacher of dermatology.

The synonyms and eponyms are complete and cross-indexed for ready reference. The essential nature of each skin disease, rather than an extensive clinical description of the lesion, is stressed, and the histopathological picture of the lesion, though brief, is adequate.

The chapter on the general principles of therapy is especially informative and useful to the practitioner as no group of diseases is more poorly treated by the busy doctor than is that embracing diseases of the skin.

This volume is not a textbook or a quiz compend but can be recommended as a useful desk companion for the busy practitioner of medicine.

*Treatment and What Happened Afterward A study from the Judge Baker Guidance Center* By William Healy and Augusta F. Bronner 8 paper 54 pp Boston Judge Baker Guidance Center 1939 50 cents.

This is an able and thoughtful follow-up study of the later adjustment of 400 cases treated five to eight years previously at the Judge Baker Guidance Center. It should be noted that the title does not read "The Results of Treatment of Delinquent and Psychologically Abnormal Children in a Child Guidance Center" because no one knows what role greater maturation, improved social environment and other circumstances may have played to induce the predominantly favorable results here reported. In fact the scientific question which the authors pose for themselves cannot really be answered except by the use of control groups, and these they do not use. In that sense they have posed for themselves an unanswerable question. However sometimes unanswerable questions are the most fruitful ones in that they stimulate thought improve standards of treatment and achieve other good social results.

In these 400 cases, 207 had personality or behavior problems 137 were non-court delinquents and 56 were delinquents referred by juvenile courts. The types of personality disorder and of delinquent conduct and the sources and ages at referral as well as cases showing abnormal personality characteristics, are described.

The altogether astounding claim is made that, after five to eight years, 81 per cent (323 cases) showed favorable careers. There is a record of 95 per cent favorable careers in cases with personality and behavior problems but of 70 per cent with the non-court and court delinquents. "With regard to the 134 favorable careers which the two groups of delinquents together showed, the carefully gathered information about them indicates that in only 31 was there any recurrence at all of delinquency." Yet, as the authors argue:

Treatment of a delinquent cannot be expected in every case to render immediate and complete immunity from outbreaks of misbehavior any more than medical treatment can be hoped always to achieve immediate relief from the symptoms of a curable disease. In our treatment cases we have definitely discovered that some early repetition of delinquency especially considering the possible continuance of the stresses which originally caused the delinquency may mean very little for the longtime outcome.

Those who had serious delinquencies had less favorable subsequent careers, as a rule. Save for some types of sex offenders there was no positive relation between the type of offense and the response to treatment. Little seems to have been done for the deeply involved homosexual individuals. Prognosis depends much more on whether the delinquent has a normally balanced personality than it does on the type of the offense.

With reference to the careers of cases presenting personality and behavior problems it was found that there was no particular age level at which one might expect especially favorable or unfavorable responses to treatment.

It is alleged that the improvement cannot be due to maturation with approaching adulthood because the median age ranged from eighteen to twenty.

What is the relation of intelligence level to improvement? When the IQ was 70-79 response was unfavorable in 66 per cent of the cases at 80-89 23 per cent at 90-109 21 per cent and at 110 and above, only 10 per cent. Yet the authors make an attempt—in the reviewer's opinion unsuccessful—to explain away the plain purport of their figures. When the figures are "up their psychiatric alley" the authors tend to accept them when they are contrary they attempt to explain them away. This may be an old attribute of the human mind but it is not good science. However the authors are undoubtedly right in asserting that high IQ's may be associated with more intelligent, better-off families that offer more favorable opportunities environmentally and co-operate more willingly in treatment. The reviewer does not suggest that IQ's tell the whole story or even the major portion of it but if intelligence does not help in adjustment, — even of delinquents, — what is it good for? The current reaction against IQ's has in some quarters gone to extreme lengths.

The authors claim that the cases of abnormal personalities account for 48 per cent of the total number of failures. They conclude that "society offers little by way of effective treatment for this class of cases," and question whether the amount of money now being spent on these cases is worth while. They think they require prolonged segregation in properly adapted colonies with experimental methods of re-educative therapy. The reviewer agrees, but is inclined to add that a little more judiciously applied eugenic sterilization in rigorously selected cases might also be a desirable therapeutic agent, now altogether too little used in the treatment of such cases. All too many people seem to have a complex against viewing any social problem even temporarily and experimentally from the point of view of human heredity.

What is the upshot of this study? Great claims are made for improvement. Are they excessive claims? We have a right to view them as improved, at least until further studies with adequate control groups are forthcoming.

*Cardiovascular Renal Disease A clinicopathologic correlation study emphasizing the importance of ophthalmology* By Lawrence W. Smith M.D. Edward Weiss, M.D., Walter I. Lillie, M.D., Frank W. Konzelmann M.D., and Edwin S. Gaul, M.D. 4 cloth 277 pp., with 35 plates (76 illustrations) and 8 tables. New York and London D. Appleton-Century Company Inc., 1940 \$4.50

The authors, three pathologists, an ophthalmologist and an internist, have collaborated in the production of a clinicopathological correlation study. Four chapters deal with hypertensive cardiovascular renal disease, four with hypertension, one with the renal aspects of senile atherosclerosis and three with nephrosis, including eclampsia and pyelonephritis. A final chapter discusses the place of the laboratory in the diagnosis and prognosis of cardiovascular renal disease. Typical illustrative case histories, clinical findings and pathological reports are presented in detail throughout. The resultant pooled data are of the sort much in demand by pathologists and many clinicians. No claim is made for originality.

The only adverse criticism to be made of this careful and laboriously pieced-together work is its insubstantial exhaustiveness for the specialist, and the lack of sufficient

therapeutic applicability for the practitioner. The typography and illustrations, and the charts in the appendix of the volume, are excellent.

*Les perforations digestives de la fièvre typhoïde—prognostic, diagnostic et traitement* By Jacques Dor. 12°, paper, 134 pp., with 9 illustrations. Paris: Masson et Cie, 1939. 24 Fr. fr.

The author of this short monograph was struck with the importance of intestinal perforations in typhoid fever and with the very poor results of treatment in these conditions. This complication he estimated to occur in about 3 per cent of all cases and in about 30 per cent of all the fatal cases. The prognosis for recovery without operation is estimated to be 5 per cent. He collected 144 cases treated by various surgeons in Marseilles and found that only 18 recovered, a mortality of 87 per cent. The average mortality in other series was found to be 73 per cent, the best figure was about 50 per cent in a small series. Some of the lower figures were found to be misleading.

The author then goes on to review the clinical, pathological and surgical aspects. Particular emphasis is placed on early diagnosis and immediate operation, since most of the fatalities result from delaying operative intervention. The indications for various types of operative procedure are given. The problem of recurrent perforations is also considered.

The volume is well printed and is written in simple readable French, with references, as usual, limited almost entirely to French writings. Since typhoid fever is still an important cause of death in many communities in this country, this little brochure should be of interest to some surgeons.

*Traité de l'immunité dans les maladies infectieuses* Jules Bordet. Second edition. 4°, paper, 879 pp. Paris: Masson et Cie, 1939. \$3.00.

This is the second edition of the classical work first published by Professor Bordet just twenty years ago. When the first edition appeared, this book, together with that by Metchnikoff and the collected papers of Ehrlich, were the only available comprehensive treatises on immunological problems and became standards which every immunologist had on his shelf. Even at that time Bordet's book was so much the most complete and critically unbiased that it rapidly attained a commanding position in the literature of this subject. A formidable amount of information has been gained in the twenty years elapsing between the two editions, but Bordet has been constantly at work during this period and nothing that has been of any importance has been neglected in the present revision. The book again reflects the wisdom and broad scope of information of the writer who, directly or indirectly, has been the teacher of every modern immunologist. Bordet's authority is based upon active service in his science, which was initiated when, with other great masters of our profession, he began to publish during the latter part of the nineteenth century, and his influence has continued, undiminished by the passage of years, into our own time.

The book has few of the characteristics of an ordinary textbook or compilation, since Bordet is familiar, either by experiment or by careful scrutiny, with the matters he discusses. He retains the vitality of expanding his intellectual grasp to new discovery, and includes in this edition consideration of bacterial dissociation, antigen and antibody chemistry, theories of anaphylaxis and allergy and many other modern aspects of immunity that were unheard of when the first edition was written. He himself

has contributed to many of the fundamental immunological discoveries and, as the reviewer has often noted, unlike almost every other great investigator, Bordet has never made a serious mistake, an achievement attributable to that clarity of mind and critical integrity which continue to keep this book a classic.

It is not a book for those who wish to look up, here and there, references or minute details of experimental procedure or results. It is a comprehensive and critical survey by a great scholar who reviews his subject with mature judgment.

Being of this nature, it should be read as a series of treatises rather than as a textbook, and for this reason, it is perhaps not a serious defect that it lacks extensive references to the literature and has no index. These omissions will probably be criticized and may lessen the general popularity of the book. They will not, however, detract from the great importance of this book for the scholar of immunology.

*Injection Treatment of Hernia, Hydrocele, Ganglion, Hemorrhoids, Prostate Gland, Angioma, Varicocele, Testicose Veins, Bursae and Joints* By Penn Riddle, B.S., M.I.F.A.C.S. 4°, cloth, 290 pp., with 153 illustrations. Philadelphia and London: W. B. Saunders Company, 1940. \$5.50.

This book is a timely addition to the collective literature, for injection treatment has established itself as the most effective method of treating a great variety of lesions. The author is not overenthusiastic about injection therapy but gives a very fair evaluation of the method. Even though he describes methods for such conditions as femoral hernia, he does not recommend them as the best treatment. For hernias he favors injection mainly in those of the indirect inguinal type, and adds "No hernia with a neck over 2 cm. in diameter should be treated. [otherwise] cure is very doubtful though improvement may follow."

Few will agree on his unitarian hypothesis that fissure, fistula, hemorrhoids and pruritus ani are all due essentially to venous stasis. But this interpretation does not cause the author to deviate from the established methods of treatment, which are well presented.

The anatomy, development, diagnosis and technique of treatment are clearly enumerated so that a physician or medical student not conversant with the subject can easily follow the discussion. The book is an excellent text for the teaching of injection treatment in the clinic, and the practitioner will find it invaluable in guiding him through the details of injection of such lesions as hernia, varicocele and hemorrhoids.

There are many excellent illustrations, and the printer is in large type, which makes reading easy and a pleasure.

*A Synopsis of Surgical Anatomy* By Alexander Le McGregor, M.Ch. (Edin.), F.R.C.S. (Eng.), with a foreword by Sir Harold J. Stiles, K.B.E., F.R.C.S. (Edin.). Fourth edition. 12°, cloth, 664 pp., with 648 illustrations. Baltimore: William Wood & Co., 1939. \$6.00.

This book, now in its fourth edition, will continue to serve the needs of students, interns and surgeons in reviewing anatomical facts. Sir Harold J. Stiles, in the foreword, rightfully commends the author for the original manner in which he has presented and illustrated his subject. The book is divided into two parts, both written in a clear, stimulating fashion and illustrated with many good black and white drawings. The first part deals with normal anatomy, while the second considers abnormal anatomy.

# The New England Journal of Medicine

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VOLUME 223

AUGUST 1, 1940

NUMBER 5

## THE RENAL FACTOR IN CONTINUED ARTERIAL HYPERTENSION NOT DUE TO GLOMERULONEPHRITIS, AS REVEALED BY INTRAVENOUS PYELOGRAPHY\*

A Study of Two Hundred and Twelve Cases, with a Report of the Results  
of Nephrectomy in Nine Cases

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BOSTON

SINCE Goldblatt and his co-workers<sup>1</sup> have demonstrated that renal ischemia in experimental animals causes continued arterial hypertension not dependent on nervous connections, but probably due to a pressor substance elaborated by the affected kidney, clinicians have sought to apply this knowledge in the elucidation of hypertension in man. For instance, hypertension has been reported in association with the following conditions obstructing arterial blood flow of the kidneys: thromboarteritis obliterans of the small renal arteries<sup>2</sup>, arteriosclerotic occlusion of the main renal arteries<sup>3</sup>, compression of the main renal artery and vein, together with an intravascular muscle plug in the main renal artery, a peculiar congenital anomaly in an ectopic pelvic kidney<sup>4</sup> and compression of the renal arteries by a firm mass such as a lymphosarcoma.<sup>5</sup> Longcope<sup>6</sup> in a prolonged follow up of 22 cases of pyelonephritis found 12 with intermittent or continuous elevation of the blood pressure. Butler<sup>7</sup> reported 15 children with chronic pyelonephritis and hypertension over a period of years before diminution of kidney function. Peters<sup>8</sup> was impressed by the frequency with which pyelitis appeared as a precursor, associate or sequel to toxemias of pregnancy. Weiss and Parker<sup>9</sup> studied 100 selected cases of pyelonephritis, all necropsied and described the gross and microscopic characteristics, concluding that pyelonephritis is an important

cause of renal vascular narrowing and that hypertension when it occurs is of the Goldblatt type. Others<sup>10</sup> report a variety of urologic lesions associated with hypertension.

There is no doubt that removal of the affected kidney in a number of patients with unilateral renal disease associated with hypertension has had a marked and beneficial effect on the blood pressure, though one hesitates to say that the patients are cured until they have been observed for several years. One of Butler's<sup>7</sup> cases was that of a boy of seven with acute and chronic active pyelonephritis who had a normal blood pressure twenty months after nephrectomy. Barker and Walters's case<sup>11</sup> was that of a man of forty-two with a chronic atrophic pyelonephritic kidney, with a normal blood pressure over two months after operation. These authors subsequently refer to 4 similar cases of their own with normal blood pressures six, twelve, thirteen and sixteen months after operation. Barney and Suby's<sup>12</sup> case was that of a ten year-old girl with chronic atrophic pyelonephritis, whose blood pressure was normal twenty-one months after nephrectomy. Leadbetter and Burkland's<sup>13</sup> case was that of a Negro aged five years with an ectopic kidney, the renal artery and vein being compressed in a groove in the kidney tissue. There was also an obstructive intravascular muscular plug in the main renal artery. The blood pressure was normal eighteen months after nephrectomy, including follow up subsequent to the case report. Bartels and Leadbetter's<sup>14</sup> case was that of a woman of thirty-seven with unilateral hydronephrosis but no evidence of extensive pyelonephritis whose blood pressure was normal ten months after nephrectomy. Crab-

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tree's<sup>14</sup> case was that of a woman of twenty-seven with a unilateral pyelonephritis and constriction of the ureter, whose blood pressure was normal for ten years except for pressor responses to 160 and 190 mm on two occasions, sustained hypertension again appearing in the eleventh year after operation. Schroeder and Fish<sup>15</sup> report the results of nephrectomy for hypertension in 7 cases with unilateral renal disease. Two were improved and 2 slightly improved, but all were still actually or potentially hypertensive. The two most favorable cases showed the least evidence of vascular disease in the surgical specimens. One of the successful cases was that of a man of thirty-three with hydronephrosis and hydroureter, with constriction at the ureterovesical junction on the left and with nephroptosis, ureteral angulation and slight hydronephrosis on the right. After left nephrectomy there was a marked and sustained fall in the blood pressure for sixteen months. The other successful result was obtained in the case of a woman of twenty. The removal of a hypoplastic kidney on one side was followed by a marked and sustained lowering of the blood pressure for eleven months.

During the last four years we have included genitourinary studies in the survey of our cases of essential hypertension in general confining this part of our study to patients under fifty, and including at least an intravenous pyelogram in all new cases. Of 596 patients diagnosed as having essential hypertension, intravenous pyelograms were taken in 212, of whom 124 were women and 88 men. Classified according to degree of organic change and clinical characteristics,\* 66 cases were Grade 1, or early hypertension, 46 Grade 2, or moderate, 41 Grade 3, or late benign,

\*Hypertension Grade 1. Variable hypertension 150 to 200 mm systolic 100 to 120 diastolic occasionally falling to normal levels (140 systolic, 90 diastolic or less) with rest or sedatives occasionally under stress going above the limits noted minimal if any changes in fundi as represented by narrowing of arterioles minimal if any changes in heart or kidneys. This is early or mild hypertension.

Hypertension Grade 2. Variable hypertension 170 to 250 mm systolic 110 to 130 diastolic usually at the lower levels occasionally even lower but rarely if ever falling to normal with rest or a sedative; the fundi showing arteriovenous compression narrowing and caliber changes in the arterioles the heart showing slight if any enlargement (prominence in the region of the left ventricle) the urine showing no change or slight grades of albuminuria and minimal numbers of formed elements in the sediment the renal function being normal or slightly impaired by concentration and intravenous phenolsulfonphthalein tests. This is moderate hypertension.

Hypertension Grade 3. Variable but usually upward hypertension almost always over 170 mm systolic and 110 mm diastolic; the fundi showing arteriovenous compression caliber changes in arterioles wide light reflexes often exudates or hemorrhages in the retinas the heart usually enlarged with possibly symptoms and signs of actual or impending congestive failure or even symptoms of anginal failure the urine often showing albumin and casts renal function often impaired but actual failure (uremia) unusual cerebral accidents sometimes occur. This is late benign hypertension as a rule of many years standing.

Hypertension Grade 4. Blood pressure especially the diastolic usually very high difficulties often of recent onset in a patient almost always under fifty often under forty the cardinal sign being edema of the optic disk with or without exudate and hemorrhage cardiac enlargement and congestive or anginal heart failure often present renal impairment and failure common. This is malignant hypertension.

and 56 Grade 4, or malignant. Grading was doubtful in 3 cases.

In reviewing these 212 cases we were interested in ascertaining the incidence of deformities of the kidneys or ureters—whether congenital or acquired, whether due to infection or metabolic fault or to some other cause—which were of sufficient degree to obstruct the flow of urine or impair the renal function on one or both sides. Significant abnormalities from this point of view were found in 47 cases (22 per cent), and are shown in Table 1. The significance of the pyelo-

TABLE 1 Significant Abnormalities in 47 of the Cases Studied by Intravenous Pyelography

FINDING	NO. OF CASES
Hydronephrosis	33
Pyonephrosis	16
Stone	14
Atrophic or fetal contracted kidney or both	13
Hydronephrosis with possible aberrant vessel	7
Possible tuberculosis	2
Tumor or cyst	1

grams in 4 cases was doubtful, the remaining 161 patients either had normal pyelograms or those showing minor variations, or had chronic

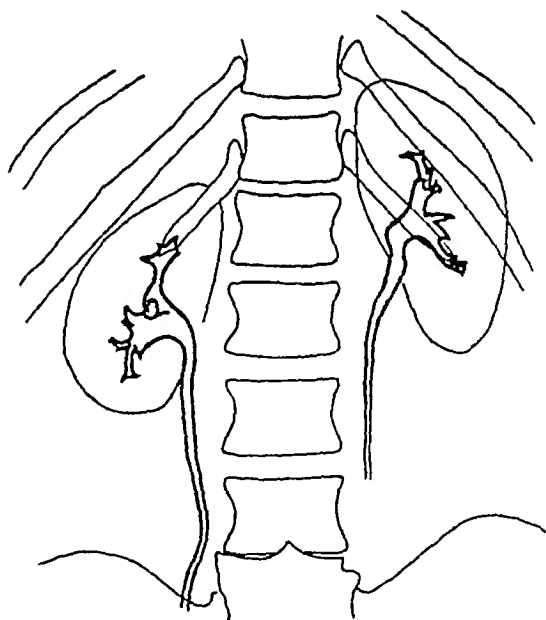


FIGURE 1

A tracing from the x-ray plate of a normal intravenous pyelogram in a patient with arterial hypertension. The outlines of the pelves and calyces are shown for comparison with those in Figures 2 and 3. The rather low right kidney is not considered significant.

vascular nephritis, the pyelograms showing small poorly functioning kidneys (Table 2).

We cannot emphasize too strongly the maintenance of a critical attitude toward the findings of intravenous urography. The kidney and pelvis on one side may be in a different plane and

appear abnormal as compared with those of the opposite side. At best the pyelogram is only the shadow of the organ studied. For instance, in one case at dorsolumbar sympathectomy a kidney, the pyelogram of which had shown it to be small and poorly functioning, was found to be rather small but normal appearing. In several

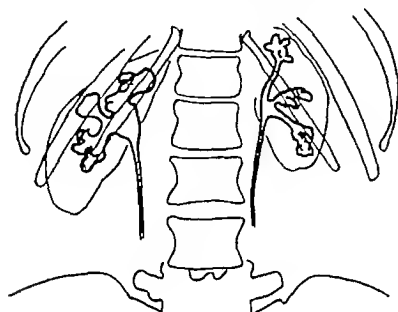


FIGURE 2.

*A tracing of a pyelogram showing evidence of bilateral pyelonephritis in a patient with Grade I hypertension found incidentally at a routine health examination. The calyces are blunted and the pelvis on the right is somewhat dilated.*

cases we have had the opportunity of examining kidneys previously depicted by urography. It is obvious that there exist considerable congenital variations in size which are apparently within normal limits as judged by gross observation, urography—both intravenous and retrograde—and split function. In order to get the true picture one must check significant intravenous urographic findings by retrograde pyelograms.

TABLE 2. Insignificant Abnormalities and Doubtful and Negative Findings in 165 of the Cases Studied by Intravenous Pyelography

Findings	No. of Cases
Poor excretion of the dye in one or both kidneys	38
Minor anatomical variations in pelvis or calyces or both	22
Kidneys small	17
Position: normal without deformity of renal pelvis	6
Calyx or pelvis slightly dilated	5
Mild abnormality of ureter	4
Small area of calcification in kidney	1
Probable calcification left renal artery	1
Doubtful	4
Negative	89

If this calcification represents narrowing of the artery, the finding may be very significant as a cause of renal ischemia, but there is no means of establishing the diagnosis anteroposteriorly.

split kidney function and urinary cultures. It is hardly necessary to mention that care must be taken when injecting the dye for retrograde visualization of the kidney pelvis since too much

dye or too much pressure may cause a normal pelvis to appear dilated. When these normal variations and possibilities of error are kept in mind and abnormal findings are carefully checked, intravenous urography is a satisfactory and fairly accurate method for indicating abnormalities of the kidneys, pelvis and ureters, provided renal function is not seriously impaired. In Table 2 are listed abnormalities considered insignificant from our point of view.

Thus 47 (22 per cent) of our patients with essential hypertension showed important abnormalities when studied by intravenous urography. Of these, 31, or 76 per cent of those from whom we obtained adequate data, had family histories of degenerative vascular disease (hypertension, heart disease, nephritis, sudden death, cerebral accidents or diabetes in siblings, parents, uncles, aunts or grandparents); the family histories were negative in 10 and uncertain in 6. This incidence is characteristic of essential hypertension in general.<sup>14</sup>

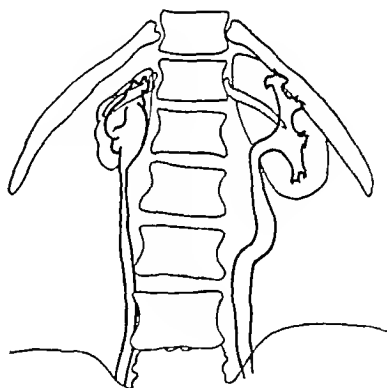


FIGURE 3

*A tracing of the intravenous pyelogram in the patient (Case 9) who has greatly benefited by removal of the right kidney showing a small kidney with a dilated and deformed pelvis on the right and a rather dilated and tortuous ureter on the left.*

As a control group we have compared 43 patients with pyelonephritis without hypertension from whom accurate family histories were obtained. Of these, 17 (40 per cent) had histories of degenerative vascular disease. The median ages of these two groups, as well as the group with hypertension and negative pyelograms, were comparable—39.0, 42.2 and 42.5 years respectively.

A unilateral abnormality of the kidney or pelvis

vis was found in 34 (72 per cent) of the 47 cases with abnormal pyelograms. In these cases we considered the possibility that the affected organ was elaborating the hypothetical pressor substance (Goldblatt syndrome). Hence, with the hope of relieving the hypertension and not because of the renal condition, which in all cases was asymptomatic, and in many of them was revealed only by the routine study with intravenous pyelogram, the affected kidney was removed in 9 cases. Our observations follow.

**CASE 1** A man of 43 with Grade 4 (malignant) hypertension had a unilateral acute and chronic pyelonephritis. He died 2 days after nephrectomy from bilateral adrenal infarction. The surgical specimen showed a large cystic hydronephrotic kidney, the parenchyma measuring from 1 to 2 mm in thickness. There was definite acute and chronic pyelonephritis, acute infection being superimposed on an old hydronephrosis. The arteries showed very slight fibrous intimal thickening. The arterioles showed moderate medial hyaline changes. No glomeruli or tubules were seen. The remaining kidney at autopsy was large, and showed acute and chronic inflammation of the parenchyma. The arteries showed slight fibrous intimal thickening, and the arterioles moderate to marked medial hyaline change with slight hyperplastic proliferation. No colloid casts were seen. Diagnosis: chronic vascular nephritis.

**CASE 2** A man of 36 with Grade 4 (malignant) hypertension appeared to have a unilateral moderate hydronephrosis. Urine culture showed *Bacillus coli* from the bladder and from the affected kidney. There was no favorable effect on the symptoms or the blood pressure after nephrectomy. The patient died of a cerebral accident 1 year and 1 month after operation. In the surgical specimen the arterioles showed medial hyaline degeneration, and the arteries fibrous intimal thickening. There was no evidence of infection. Diagnosis: chronic vascular nephritis.

**CASE 3** A man of 45 with Grade 3 (late benign) hypertension had unilateral pyelonephritis and hydronephrosis. Culture of the urine showed no growth. After nephrectomy there was definite symptomatic improvement but no change in the blood pressure. The heart showed progressive enlargement until death from a cerebral accident 1 year and 3 months after operation. The kidney removed at operation weighed 32 gm. The pelvis was dilated to 10 cm in circumference. The glomeruli were obliterated. A moderate number of colloid casts were seen, and there was lymphocytic infiltration. The arteries showed moderate to marked fibrous intimal thickening. The arterioles showed slight hyperplastic proliferation. There was no hyaline degeneration. Diagnosis: congenital aplasia and chronic pyelonephritis.

**CASE 4** A woman of 33 with Grade 3 (late benign) hypertension had unilateral renal calculi and hydronephrosis, hyperparathyroidism having been alleviated by removal of a parathyroid adenoma 3 years previously. Culture of the bladder urine showed *B. coli*, but culture of the urine from the infected kidney showed no growth. Nephrectomy was followed by slight temporary improvement in the blood pressure for 3 months after operation. One year and 11 months after operation the blood pressure had returned to the preoperative level. The surgical specimen weighed 78 gm. There were small foci of healed

pyelonephritis in which the arterioles showed hyperplastic proliferation. The arteries were negative. There was lymphocytic infiltration in the pelvis. A few colloid casts were present in the scarred areas. Most of the kidney parenchyma was intact. Diagnosis: focal pyelonephritis.

**CASE 5** A woman of 26 with Grade 3 (late benign) hypertension had a unilateral hydronephrosis. Culture of the urine from the infected kidney showed *B. coli* and *Staphylococcus aureus*. After removal of the affected kidney the blood pressure was somewhat lower for about a year. The eye grounds improved. During the 2nd year after operation the blood pressure returned to the preoperative level. There was an illness suggesting recurrent pyelonephritis in the remaining kidney. Four years after operation there appeared to be progressive increase in the size of the heart, the blood pressure remaining at about the preoperative level. The surgical specimen weighed 61.5 gm. There was marked hydronephrosis. In scarred areas there was moderate to marked medial and intimal hyalinization. There were no definite arteriolar hyperplastic changes. The arteries were negative. There was slight lymphocytic infiltration. A few colloid casts were seen in the scarred areas. Diagnosis: focal pyelonephritis.

**CASE 6** A neurotic woman of 50 with Grade 1 (mild, variable) hypertension had a cystic kidney with hydronephrosis. *B. coli* was grown from the bladder urine. For 6 months after nephrectomy there was no improvement in the blood pressure. The surgical specimen weighed 119 gm. There were gross cysts up to 3 cm in diameter. There was scarring in the region of the cysts. A few tubules showed colloid casts. The arteries showed slight fibrous intimal thickening. The arterioles showed medial hyaline changes, but there was practically no hyperplastic proliferation. Lymphocytic infiltration was slight. Diagnosis: chronic vascular nephritis.

**CASE 7** A woman of 41 had Grade 1 (mild) hypertension and an atrophic non-functioning kidney. A culture of the urine showed no growth. The blood pressure showed no change during one year after nephrectomy. The surgical specimen weighed 7 gm. It showed congenital atrophy. The arteries showed marked fibrous intimal thickening. The arterioles were negative. There was no lymphocytic infiltration. Diagnosis: probable congenital atrophic kidney.

**CASE 8** A schoolgirl of 19 with Grade 1 to 2 (mild to moderate) hypertension had a contracted kidney with poor function on the left side. There was a history of pyelitis 9 years previously. Hypertension was known to have been present for only 5 months, having been found incidentally. Cultures of the urine from both kidneys were negative. Six weeks after nephrectomy the blood pressure was not significantly lowered. Six months later the blood pressure was somewhat lower as a result of sulfocyanate therapy, but it was evident that operation had not significantly altered the condition. The surgical specimen weighed 14 gm. The arterioles showed marked hyperplastic proliferation in scarred areas, but no hyalinization. The arteries showed moderate fibrous intimal thickening. Lymphocytic infiltration was very slight. Colloid casts were seen in the tubules in scarred areas. Diagnosis: chronic pyelonephritis.

**CASE 9** A girl of 17 with Grade 4 (malignant) hypertension showed edema of the optic disks and exudate and hemorrhages in the retinas, and had a contracted, pyelonephritic kidney. Hypertension had been found during an illegitimate pregnancy 4 years previously. For 1 year





hyperplastic changes, lymphocytic infiltration and colloid casts in the tubules. Although most of the other cases showed pyelonephritis, usually with hydronephrosis, the vascular changes were those seen in ordinary vascular nephritis, that is, they consisted of medial hyalinization of the arterioles and fibrous intimal proliferation of the arteries, or if there were hyperplastic changes, they were of insufficient severity to have had any effect. The fact that one of these two cases (Case 9) has been much improved by nephrectomy suggests that the arteriolar hyperplastic change plays a dominating role in the production of the hypertension. The fact that the other case did not respond may possibly be explained by Weiss and Parker's theory that the nephrectomy had been done after the vicious circle—pyelonephritis leading to hypertension, which in turn leads to vascular nephritis in the other kidney—had been established.

As intimated above, we have not sufficient data on the incidence of hypertension and of renal lesions in the general population to reach a mathematical estimate of how often such a renal lesion may be merely incidental. Furthermore, no clinical tests now available enable one to predict accurately the character of the changes in the renal vessels, or to determine whether the hypertension, if due to renal ischemia on one side, may have induced vascular disease in other tissues, including the originally unaffected kidney. In considering nephrectomy, the best possible judgment after careful study is not very good, as demonstrated by only one strikingly favorable result in our group of 9 cases, and only two in the group reported by Schroeder and Steele.<sup>9</sup>

In exercising this clinical judgment, the age of the patient and the duration of the hypertension should be considered. In general, it may be said that one should not advise nephrectomy for a unilateral renal lesion when associated with hypertension in women over forty-five or men over fifty, since after these ages the onset of continued arterial hypertension of unknown etiology is likely to appear. The ages of the cases in the literature with apparently successful results referred to above range from childhood to forty-two. It is generally impossible to estimate accurately the duration of hypertension. However, one would suppose that if it has been known to have been present for a long time, nephrectomy is contraindicated, since vascular changes in the other kidney might be expected. Nevertheless, in our only favorable result the patient was known to have had hypertension during an illegitimate pregnancy four years previously, while

in Case 8, closely similar both clinically and pathologically, hypertension was known to have been present for only five months, although pyelitis had occurred nine years previously. Presumably, the younger the patient and the more recent the onset of hypertension, the better the chance of a favorable result following nephrectomy.

One cannot afford to overlook the factor of congenital predisposition in patients with continued arterial hypertension. Patients with chronic pyelonephritis, both active and inactive, and those with lesions obstructing the urinary outflow have been followed for many years without the appearance of continued arterial hypertension. The difference between these patients and those with similar urologic lesions and also continued arterial hypertension may lie in the degree of congenital predisposition. Our control group of patients with pyelonephritis but without hypertension referred to above is small. Nevertheless, the family histories suggest that a predisposition to degenerative vascular disease was present in only 40 per cent, an incidence characteristic of 100 miscellaneous ward patients in whom no vascular disorder was present.<sup>10</sup> On the other hand, the patients with such deformities and with continued arterial hypertension had family histories indicating a tendency to vascular disease in 75 per cent, an incidence characteristic of any series of patients with continued arterial hypertension. Pyelonephritis, hydronephrosis, calculus disease, cyst, tumor or external obstruction of the urinary tract, with or without infection, if not incidental, may be merely participating or precipitating causes initiating the pressor responses in patients predisposed to arterial hypertension. Thus, unilateral renal disease may precipitate continued arterial hypertension in a congenitally predisposed individual sooner than the natural factors associated with the menopause or with advancing years. Crabtree's<sup>14</sup> case is interesting in this connection in that removal of a kidney for unilateral renal disease at the age of twenty-seven was followed by freedom from hypertension for ten years, except for two observations. In the eleventh year, however, persistent hypertension reappeared. This suggests that nephrectomy removed a precipitating cause, although the congenital predisposition remained.

#### CONCLUSIONS

Forty-seven (22 per cent) of 212 patients with continued arterial hypertension not due to glomerulonephritis showed congenital or acquired deformities of the pelvis or ureters by urography.

The deformity in the pyelogram was unilateral

in 34 (72 per cent) of these 47 cases, or 16 per cent of the 212 cases studied

Such deformities are often incidental but if significant in the etiology of the hypertension probably represent a participating or precipitating, rather than a major, factor

Surgical removal of the presumably offending organ in 9 cases resulted in marked improvement in the blood pressure and the symptoms for one year and ten months in 1 case, although this patient still remains definitely hypertensive.

In cases of unilateral renal disease associated with persistent hypertension the decision to remove the affected kidney, with the hope of curing or modifying the course of the hypertension is based on three assumptions that the lesion is not incidental that there is no vascular disease in the remaining kidney, and that one will not be faced with recurrent pyelitis in the remaining kidney

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NEUROGENIC DYSFUNCTION OF THE BLADDER DUE TO SPINAL ANESTHESIA\*

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NERVE damage resulting from spinal anesthesia is fortunately a rare complication but apparently it is much commoner than is generally recognized. Of the various sequelae of spinal anesthesia which have been reported paralysis of the bladder appears to be one of the most serious. In the majority of the cases the bladder dysfunction persisted over a period of many months or years, and death not infrequently occurred as a result of infection of the urinary tract. However as the reports deal primarily with the neurological and not with the urological aspect of the cases, it seems worth while to report a case in which the patient recovered following resection of the presacral nerve. This case is, so far as we know the only one so treated although it appears that the operation might have been successfully applied to other cases which have been reported.

It is interesting that the neurologic lesions resulting from spinal anesthesia are extremely varied both in character and in severity. Loesser<sup>1</sup> reports

5 cases of peripheral neuritis affecting isolated peripheral nerves which he had seen in one year. These cases followed the giving of small doses of procaine. Likewise, cases of ocular paralysis lasting several weeks or more have been reported.<sup>2</sup> Smith<sup>3</sup> saw a case of incomplete transverse myelitis following the use of Spinocain. Hyslop<sup>4</sup> reports a case of aseptic meningitis resulting from the administration of 200 mg of Nupercaine. One of us (E. L. P.) has seen a similar case following the giving of 150 mg of novocain. Ferguson and Watkins<sup>5</sup> report 14 cases of injury to the cauda equina which they had personally observed and have also collected 16 other cases from the literature. In these, the most striking and most serious symptom was immediate retention of urine, followed at a later period by incontinence. The patients continued to have residual urine and difficulty in urinating for periods varying from several weeks to over two years. The less serious symptoms in this group consisted of loss of anal tone, an area of saddle anesthesia and changes in the reflexes of the legs. In some cases cystometric and cystoscopic studies were made after a period

Presented at meeting of the New England Branch of the American Urological Association, Boston, March 2, 1939.  
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of several months and the patients were found to have trabeculated, hypertonic bladders, associated with a variable amount of residual urine. In the proceedings of the Royal Society of Medicine for 1936-37, Critchley<sup>7</sup> reported 17 cases of neurologic sequelae of spinal anesthesia. Eight of these patients had paralysis of the bladder and only 3 recovered spontaneously. Critchley states, "A very significant number of nervous sequelae are completely overlooked by both the surgeon and the anesthetist." This opinion has been expressed by numerous other writers and appears to us to be wholly justified. Other cases of disturbance of the bladder mechanism and other neurologic manifestations have been reported by Boisseau,<sup>8</sup> Nonne and Demme,<sup>9</sup> MacLachlan,<sup>10</sup> Brock, Bell and Davison,<sup>11</sup> Lindemulder,<sup>12</sup> Ashworth<sup>13</sup> and others.\*

### CASE REPORT

The patient (No. 75570), a robust looking man of 60, was admitted to the Lynn Hospital on November 9, 1938. Eight weeks previously he was operated on in another hospital for acute appendicitis under spinal anesthesia, given by an experienced anesthetist who used 100 mg of novocain and 14 mg of Pontocain. The operation was uneventful except that following it the patient was unable to void. He was treated both by intermittent catheterization and by continuous drainage. For several weeks before entry he had been at home and had been catheterizing himself several times a day. During this time, although he had discomfort when his bladder was full, he had been unable to void. Mecholyl had been tried without improvement. Except for marked constipation and weakness he had no symptoms. The past history was irrelevant. At no time prior to the operation had there been difficulty in urinating, frequency or other symptoms suggesting disturbance of the urinary tract.

Tests made during physical and neurological examinations had to be repeated over and over on account of the patient's unreliability. The significant findings follow. The rectal sphincter had normal tone and the prostate gland was not enlarged. The deep reflexes of the upper extremities were diminished, the abdominal reflexes were diminished to absent, the deep reflexes of the lower extremities were hyperactive, and there were a Babinski and ankle clonus on the right. Sensation of light touch, vibration sense and muscle position sense of the lower extremities were definitely impaired. Wassermann tests of the blood and spinal fluid were negative. Lumbar punctures done on two occasions showed a large number of red blood cells and no white cells. There was no xanthochromia, and it was uncertain whether or not the presence of blood was caused by the trauma of the punctures. The dynamics, sugar content and gold sol curve were normal, the globulin negative, and the total protein was 200 mg per cent at one time and 125 mg at the other. The urine examination

showed evidence of marked sepsis and consequent diminished renal function. The rest of the laboratory examination was negative. Cystoscopic examination showed no trabeculation of the bladder, no prostatic obstruction and no hypertrophy of the internal sphincter. Neither did there appear to be any funneling of the bladder neck. The resistance of the sphincters to the passage of the cystoscope and the sensation in the urethra appeared to be diminished. Intravenous pyelograms showed normal kidneys and bladder.

On admission the patient was put on catheter drainage. Preoperative cystometric studies were made the day after admission and again 19 days later (Fig. 1). The findings

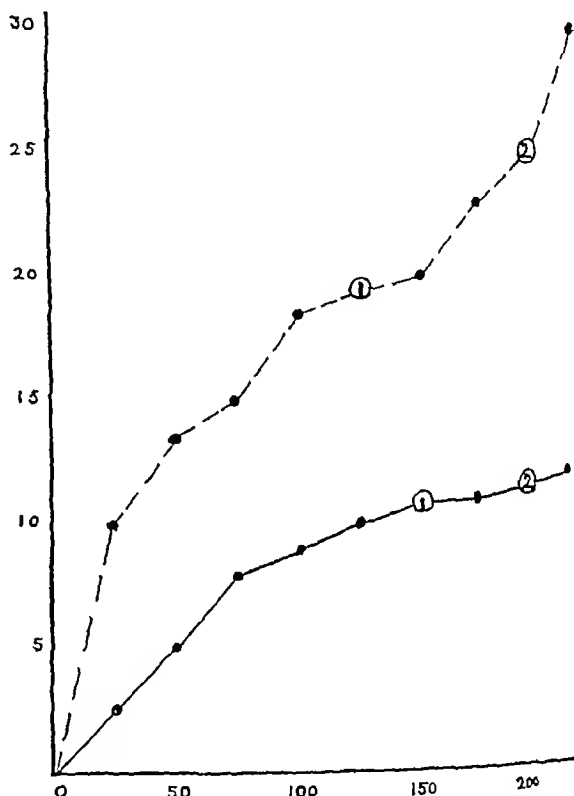


FIGURE 1 Cystometric Studies

The solid line indicates the preoperative readings, the dotted, the postoperative ones. At (1) occurred the first desire to void, and at (2), the pain of fullness. The abscissa denotes the volume of the injected fluid, expressed in cubic centimeters, and the ordinate, the intravesicular pressure, expressed in centimeters of water.

on both occasions were essentially the same: the patient felt the desire to void when 100 to 150 cc. of fluid had been introduced into the bladder and had severe pain after the introduction of from 200 to 225 cc. A presumptive diagnosis of neurogenic dysfunction of the bladder was made. It was believed that the patient might have had a cord injury with particular involvement of the posterolateral tracts and probably some radicular injury.

On December 1, after 3 weeks of catheter drainage, the sepsis in the urinary tract had greatly improved and the catheter was removed. The patient, however, was still unable to void. As 2½ months had elapsed since he first developed acute retention, it appeared that the assumed damage to the spinal cord was permanent. Accordingly, on December 2 a presacral neurectomy was performed.

\*In a recent personal communication to the author Dr. Charles E. Rieser of Atlanta, Georgia, cites a case which is almost identical to the one reported here. Dr. Rieser's case was that of a twenty-six year old man who had had an appendectomy under spinal anesthesia in November 1939. Following this he had retention of urine for three months which was treated by self-catheterization. No obstruction was seen at the bladder neck and the neurological and spinal fluid findings were negative. The retention was relieved by a transurethral resection of the internal bladder sphincter.

The patient made an uneventful convalescence. A cystometric study made 8 days after the operation showed definite increase of tone, the curve being on the average about 10 cm. of water higher than the preoperative ones (Fig. 1). The catheter was removed on the 10th post operative day and the patient was able to void spontaneously for the first time. There was considerable residual urine at first, but each day this became less marked until on the day of discharge, December 21 it was reduced to 190 cc.

Following discharge the patient did well. He voided once at night and every 4 hours by day. The stream however, lacked force and the patient could empty his bladder better in the sitting position. When last seen 7 months after discharge, he had no residual urine and the infection had almost disappeared. He complained of marked constipation and pain at the base of the spine, and stated that neither of these symptoms had been present prior to the first operation.\*

It was presumed that the paralysis of the bladder in this case was due directly to nerve damage resulting from the spinal anesthesia. Why nerve damage occurs in some cases and not in others is hard to explain. From the experimental work done on this subject it appears that various cocaine derivatives have a destructive effect on nerve tissue, depending directly on their concentration. As we are dealing here with the urological rather than the neurological aspect of the subject, it will be sufficient to state that Davis Haven Givens and Emmett<sup>14</sup> and Lundy Essex and Kernohan<sup>15</sup> produced lesions of the cord and spinal nerves in dogs with the intraspinal injection of procaine, and that MacDonald and Watkins<sup>16</sup> produced similar nerve destruction in cats by the same method. In the human cases which suffered from neurological complications, autopsy showed degenerative nerve changes similar to those found in the experimental animals. There has been but little work done on changes in the spinal fluid following the subarachnoid injection of cocaine derivatives in human subjects but from the work of Iason<sup>17</sup> it would appear that there are definite, though not marked, changes in a high percentage of cases. Therefore it seems reasonable to suppose that some individuals have a greater susceptibility than others to the myelolytic properties of those substances and consequently are more likely to develop serious nerve damage. As the nerves supplying the bladder are the ones subjected to the greatest concentration of the anesthetic agent, it is not surprising that they are often damaged to a greater extent than are the other nerves. From the experimental work mentioned in this report it is likely that temporary as

well as permanent nerve damage may be produced by the various cocaine derivatives. Furthermore, it seems probable that similar mild cases of bladder paralysis may occur more frequently than is realized but because of their spontaneous recovery and lack of other obvious neurologic lesions remain undiagnosed.

The successful result following presacral nerve resection in this case may be due to two factors: first the sensation of the bladder was impaired little if at all, secondly, the diagnosis was made and treatment instituted at an early stage. This latter factor, as one of us (E. L. P.<sup>18</sup>) has already pointed out seems to be the essential point in the handling of the neurogenic bladder. The classic cord bladder where there is complete loss of tone and sensation associated with funneling of the bladder neck is usually an end result. In this type of case the chronic overdistention that has developed has permanently damaged the bladder, and in spite of prolonged catheter drainage it remains hypotonic and the chances of a successful outcome are poor. On the other hand in early cases, as in the case under discussion, the bladder rapidly regains its tone on catheter drainage. When this occurs the cystometric curve is no longer of the hypotonic type. Thus the cystometric readings must be considered in connection with the phenomena of compensation and decompensation, with the realization that where compensation occurs the prognosis is good.

Urinary sepsis is of the greatest importance in these cases. This is best controlled and the function of the bladder best preserved by the use of an indwelling urethral catheter. In this connection there are two extremely important points which are applicable to all cases of retention of urine. In the first place, the catheter used must be a small Foley catheter which will remain in place without a constricting band of adhesive tape and will allow free outward drainage of urethral secretions. In the second place, the drainage system must be closed so that infection does not enter from the outside, and so that irrigation may be carried on without disconnecting or opening the system. If these two prerequisites are adhered to, we believe the results will be fully as good as with the use of the ingenious but complicated system of tidal drainage described by Munro.<sup>19</sup>

#### SUMMARY

The case is reported of a sixty year-old man who was entirely well until an appendectomy was performed under spinal anesthesia. Following this

\*The patient when seen on July 18, 1940, one year and four months after his first operation, felt well and had gained weight. He still complained of dull pain at the base of the spine and marked constipation and of some difficulty in voiding. The knee jerks were hyperactive and the rectal sphincter slightly relaxed. There was 15 cc. of residual urine and the sediment was negative.

operation he had complete retention of urine lasting for two and a half months. Since a complete study of the case failed to show any other cause for this retention, it was assumed that the bladder dysfunction was due to nerve injury as a result of the spinal anesthesia. The retention of urine was relieved following a presacral nerve resection and the patient has remained well.

The literature on this subject is reviewed, and it is suggested that minor degrees of nerve damage may result more frequently from spinal anesthesia than is usually thought to be the case.

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## RECURRENT GALLSTONE ILEUS\*

## Report of a Case

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CASES of intestinal obstruction due to gallstones occur often enough to make single case reports undesirable unless attended by some unusual feature of interest. The last attempt to estimate the reported cases was in 1925, when Moore<sup>1</sup> set the figure at about 400. In the last ten years, approximately forty-eight articles in English and eighty-nine in foreign languages have been published on this subject, many of which added several or more cases to those already reported.

The following case is rare because the patient, a seventy-nine-year-old woman, suffered from two episodes of acute intestinal obstruction within a three-month period. Each required jejunotomy and was followed by recovery. In 1929, Holz<sup>2</sup> listed but 5 cases in which gallstone obstruction had occurred in the same individual more than once, in 3 of these the second stone was removed during immediate convalescence from the first operation. Two cases of double obstruction, the recurrence coming within several days after operation, were also reported by Downes<sup>3</sup> and by

Pybus,<sup>4</sup> but were not included in Holz's enumeration. In 1938, Schwarke<sup>5</sup> added another case, occurring in a sixty-nine-year-old woman, with recovery after operation. Thus in 5 of the 8 cases the second attack of ileus complicated the first convalescence. Four individuals survived, the oldest being a seventy-two-year-old woman.

The present case is the ninth to be reported and the patient is the oldest individual in whom recovery has occurred.

## CASE REPORT

A 79-year-old widow had had a radical mastectomy 15 years prior to her present illness. At that time routine preoperative x-ray examination revealed what was interpreted as a single large stone in the gall bladder. The patient had been troubled with intermittent gaseous indigestion for a great many years, usually following the ingestion of fatty food or pork. Occasionally she had experienced a sense of pressure across the epigastrium. However, she had never had a frank attack of cholecystitis, biliary colic or jaundice.

The patient was first seen in March, 1939, about 3 weeks prior to hospital entry, with pain in the left lower quadrant of the abdomen. Examination revealed only direct and rebound tenderness in the left lower quadrant. The diagnosis of diverticulitis seemed most probable. A barium enema on March 9 was unsuccessful because the patient

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could not retain the barium. On the following day she expelled a moderate sized gallstone from the rectum (Fig. 1). It had two facets, indicating that there were at least two more stones to be accounted for.

During the 2 weeks prior to admission on March 19 the patient had mild intermittent, colicky pain across the lower abdomen, chiefly on the right side. Five days before admission she passed a second hard object which felt like a stone but was not recovered. Two days before admission she commenced to have similar pain across the abdomen just below the umbilicus, associated with persistent vomiting. There was no tenderness distention or audible hyperperistalsis. On the following day hospital admission was recommended because of persistent symptoms. At the time of entry the bowels had not moved for 2 days.

On physical examination at entry the patient was somewhat dehydrated. She was vomiting greenish intestinal

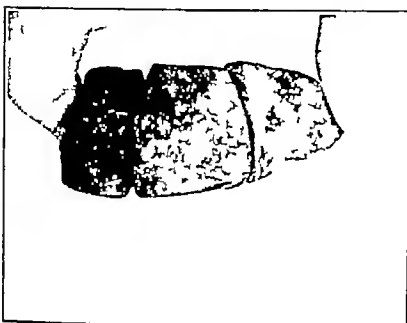


FIGURE 1 Photograph of Stones

*The stone on the right caused obstruction but its weight and diameter were less than the defecated stone which is on the left. The stone in the middle caused the second obstruction. A fourth stone was lost at defecation.*

contents without fecal odor. She was quite obese, but appeared younger than her stated age. The blood pressure was 174/98, the pulse 86, and the temperature normal. The heart rhythm was regular but there was a moderate blowing apical systolic murmur. The lungs were clear. The abdomen was very obese. The patient was unable to say whether the abdomen was any larger than normal but there appeared to be some degree of distention, although it was far from tense. There was moderate tenderness over the lower abdomen and a few high pitched peristaltic tinkles were heard above the umbilicus. An admission diagnosis of high intestinal obstruction probably in the jejunum and due to an impacted gallstone, was made. A scout plate of the abdomen showed several dilated loops of small bowel and an indistinct but definite ovoid shadow within the lumen of the intestine on the left side of the abdomen which was assumed to be an impacted gallstone (Fig. 2).

The patient's condition was not good. The nonprotein nitrogen was 54 mg. per 100 cc., the carbon dioxide combining power 42 vol. per cent and the blood chlorides 379 mg. per 100 cc. The urinary output was scanty. In addition there was a history of moderate dyspnea some orthopnea and a productive morning cough. The patient had been treated for high blood pressure during the pre-

vious 3 years. Accordingly a day was spent in improving her condition by intestinal decompression and correction of deranged fluid and chemical balances.

On March 21 a jejunotomy was performed and an impacted gallstone was removed from the mid-jejunum. The operation was done under spinal anesthesia and was followed by a transfusion. The stone was milked proximally for 15 cm. prior to removal. No search was made for additional stones nor was the region of the gall bladder palpated.

The patient made a very satisfactory convalescence and was discharged on the 14th postoperative day. In retrospect, it is apparent that it would have been well to have palpated gently the gall bladder and the intestine proximal to the site of obstruction at the time of operation.

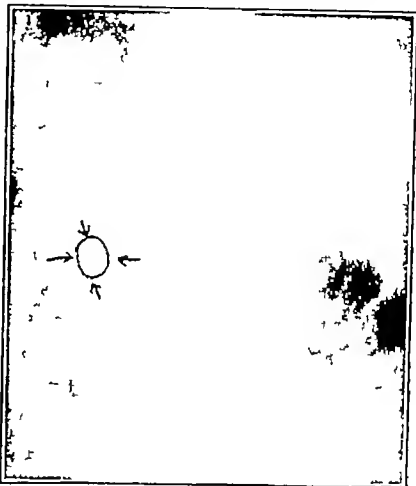


FIGURE 2 Scout Plate Prior to the First Operation

*The shadow of the stone while definite was faint and would have been lost on reduction hence it has been marked. Several loops of dilated small bowel overlie the third lumbar vertebra.*

For 2½ months the patient did very well and resumed the care of her 99 year-old mother. On June 15 she noticed a sudden loss of appetite and felt somewhat nauseated but did not vomit. She had very mild pain in the right para umbilical region. On the same day she had four or five watery bowel movements but no vomiting. I examined her on the 2nd day of this illness because of persistent nausea, mild upper-abdominal cramps and diarrhea. There was some slight distention but no spasm or tenderness. A few high-pitched, metallic, peristaltic sounds were audible over the right side of the abdomen. It seemed clear that the patient had partial intestinal obstruction probably due to adhesions rather than to a second impacted gallstone, since three gallstones had presumably been already accounted for.

At any rate, the patient refused to be hospitalized until the following day by which time she had vomited once. The abdominal examination was less definite than at the first entry. There was no definite distention. There

was no muscle spasm and only slight tenderness in the right para umbilical region. The patient was in better general physical condition than at first entry. The blood pressure was 126/80. There was no apparent acidosis or dehydration. The white-cell count was 8000, the values for blood chemical constituents were normal. A scout plate of the abdomen revealed a few somewhat dilated loops of small bowel. Gas was present in the large intestine, it was apparent that the obstruction was not complete. The patient was unwilling to be operated on and was having daily liquid dejections. Accordingly a Miller Abbott tube was inserted into the stomach and decompression attempted. This was only partly successful because the balloon broke. Administration of 100 per cent oxygen was poorly tolerated, and during a 12 hour period the girth of the abdomen increased from 102 to 105 cm. The patient vomited when the duodenal tube was clamped, and commenced to have slight rebound tenderness to the right of the umbilicus. A check scout plate showed a slightly increased amount of gas in the small bowel and also in the large bowel.

Finally, after 3 days of decompression and fluid therapy, a second laparotomy was done under spinal anesthesia. Another impacted gallstone was removed some distance from the site of the first stone. An omental graft was placed over the bowel wound to minimize adhesions and kinking.

The patient had a stormy convalescence but was finally discharged on the 22nd postoperative day. She had ileus requiring gastric drainage for 15 days. There was also major wound sepsis with profuse, purulent discharge and infection at the fascial level. It was thought that this infection might have been avoided by the use of a cellophane lined pad, as advocated by Lahey.<sup>6</sup> It was noteworthy that during convalescence, until 2 days prior to discharge, the patient continued to pass stools which were very light in color, although she had no jaundice and the stools were well formed. The explanation of this lessened amount of bile was not evident.

Six months later the patient was symptom free and was performing her usual duties. The operative scar was solid.

Intestinal obstruction is a common condition. The frequency of gallstone ileus is best stated in terms of its incidence in relation to all cases of intestinal obstruction. Thus Bennett<sup>7</sup> found 28 examples of gallstone ileus in 3064 cases of intestinal obstruction, an incidence of less than 1 per cent. Balch<sup>8</sup> tabulated 10 cases (2 per cent) of 502 obstructions seen at the Massachusetts General Hospital. It suffices to say that of all cases of intestinal obstruction, from 1 to 2 per cent are due to gallstones. A characteristic feature of gallstone obstruction is clearly demonstrated by the fact that many of the reported cases presented a picture of nonsurgical obstruction of a temporary or incomplete nature, with disappearance of symptoms after the passage of the gallstone by anus. Thus in Wagner's<sup>9</sup> total of 334 cases, 93 patients rid themselves of the cause of their obstruction by defecation of the offending stone. However, if surgical intervention is delayed, in the hope that such a favorable outcome may result from nonsurgical measures, an already formidable mortality rate will become even greater. It is

important, nevertheless, to bear in mind that this is an obturation type of obstruction. Hence, in a number of cases the cure is spontaneous. Often such episodes occur in patients who do not consult a physician at the time.

#### AGE

One of the reasons for the high mortality is that the condition occurs chiefly in people of advanced years. In Balch's series the average age was sixty-six. Wortmann<sup>10</sup> reports its occurrence in a twenty-five-year-old woman. Dulin and Peterson<sup>11</sup> had a patient of eighty-three who survived operation.

#### SEX

All observers have been unanimous in finding a much higher incidence in women, out of proportion to the more frequent occurrence of gallstones in women. The ratio is about 5:1.

#### MORTALITY

The mortality rates in the literature vary more widely than the figures on any other phase of the subject. Moller<sup>12</sup> had an 89 per cent mortality in 22 cases, his group of cases is one of the largest on record. The figure given by Grey Turner<sup>13</sup> is extraordinarily good, with 8 recoveries out of 10 private cases. The average figure is around 50 per cent, and this is the mortality rate in the 10 cases seen at the Salem Hospital.

#### MECHANISM OF OBSTRUCTION

Practically all gallstones that cause intestinal obstruction make their way into the intestinal tract through a cholecystoenteric fistula. The first and second portions of the duodenum are the commonest sites of entry. In a rare case, the stone may pass into the duodenum through a tremendously dilated common duct, or a fistula may occur between the common duct and the duodenum. Thompson<sup>14</sup> has tabulated 10 cases of duodenal obstruction from stones lodged partly in the gall bladder and partly in the duodenum. The stomach or other portions of the bowel may be the site of the fistula. Surgical oddities are those fistulas emptying into the pleural or pericardial cavity, pelvis of kidney, gravid uterus and so forth. Vomiting of gallstones has occurred a number of times.

Barnard<sup>15</sup> states that stones less than 2.5 cm in diameter are passed spontaneously. Gutmann<sup>16</sup> estimates that 50 per cent of stones ulcerating into the bowel cause obstruction. Many factors in addition to the size of the stone influence the occurrence of obstruction. Since this is an obturation type of obstruction, the block may occur at any point from the entrance of the fistula into the intestine to the anal canal. Cases have been reported in all portions of the bowel. The

commonest site is naturally the ileum since this is the narrowest portion

Many coincident factors have a bearing on whether or not obstruction occurs. Enlargement of a stone during its passage, kinks in the bowel because of adhesions, the presence of a Meckel's diverticulum, a slow rate of peristalsis or localized spasm of the bowel wall brought about by the gallstone may precipitate obstruction in some cases where the stone is borderline in size. In the present case, the first obstruction was caused by a stone the diameter and weight of which were less than those of a previously defecated one.

Thus, as the stone makes its way along the intestinal tract, there may be one or more episodes of partial, temporary obstruction before its final arrest. The obstruction is rarely complete hence a marked degree of distention is not present. Since at the outset the block is merely mechanical bowel circulation is rarely jeopardized. Therefore tenderness is minimal unless a complicating peritonitis is present.

#### SIZE OF STONE

Stones large enough to occlude the intestinal lumen are usually the size of a walnut, according to Wangenstein.<sup>17</sup> The largest recorded stone was removed successfully from the transverse colon of an eighty-one year-old man by Grey Turner and measured 70 by 60 by 170 cm. In our case, the defecated stone measured 3.2 by 3.0 by 2.0 cm and weighed 13.2 gm. While the first obstructing stone measured 3.0 by 3.0 by 3.1 cm and weighed 12.7 gm., the second one measured 3.2 by 3.2 by 2.9 cm and weighed 19.0 gm. Wangenstein emphasizes the role of spastic obstruction by calling attention to a stone which was so small that it weighed less than 4 gm., yet caused fatal obstruction. Borman and Rigler<sup>18</sup> report a fatal ileus due to a stone measuring 2.8 by 1.8 cm.

#### SYMPTOMS

In the majority of cases the preoperative diagnosis is intestinal obstruction. In 10 cases recently reported by Wakefield, Vickers and Walters,<sup>19</sup> of the Mayo Clinic, the specific type of obstruction was not diagnosed preoperatively in any case. Thus the paramount symptoms are simply those of obstructed bowel, that is, pain, vomiting and obstipation.

However, the symptomatology of gallstone ileus is unusually variable and misleading because of the mechanism of the obstruction. In the majority of patients, a history of previous biliary-tract complaints is elicited. Such complaints vary from chronic dyspepsia and belching to repeated attacks

of biliary colic, or cholecystitis with pain in the right upper quadrant of the abdomen, nausea and vomiting. These are symptoms which precede the extrusion of the stones into the intestinal tract. It has been suggested that fewer cases of gallstone ileus will be encountered in the future, because there will be fewer chronically inflamed gall bladders left in the body to form adhesions and later fistulous connections with adjacent organs.

When the stone passes into the intestine, the event may be signalized by a definite bout of severe upper abdominal pain and vomiting which subsides after a few days. On the other hand, the transit may be unaccompanied by symptoms.

Once in the intestine, the stone characteristically causes cramps as it makes its downward passage. In many cases, prior to the final obstruction which necessitates surgery, there will have been one or more episodes of varying degrees of obstruction manifested by intense cramps together with vomiting and obstipation. Because of ball valve action and increasing peristalsis, the temporary halt is overcome, symptoms subside, and progress is resumed until the lower ileum is reached, wherein complete, persisting obstruction often ensues. In the present case, the first symptoms were those of colic, slight distention and tenderness in the left lower quadrant so that a diagnosis of diverticulitis with spasm was suggested. After a barium enema a faceted gallstone was passed by anus. During the next two weeks the patient experienced intermittent colic, which ceased after the expulsion of the second stone, only to be followed by a complete obstruction of the small bowel from a third stone, the diameter of which was no greater than that of the first.

Even when the final obstructing point is reached, the symptoms are not so pronounced as those in other types of obstruction. A number of authors<sup>11, 20-23</sup> comment on the lack of distention indicating that at least some gas is able to pass the stone. Nor is tenderness a common finding. A mass can be palpated infrequently. Powers<sup>23</sup> believes that tenderness beneath the right costal margin suggests a diagnosis of gallstone ileus.

Thus, another reason for the high mortality is found in the equivocal character of the premonitory symptoms and the actual ileus. Frequently elderly patients are hospitalized only after many days of obstructive symptoms.

#### DIAGNOSIS

The diagnosis in most cases is intestinal obstruction the cause being undetermined. The abdominal flat x-ray plate occasionally reveals an intraluminal shadow which suggests a gallstone



Lowman and Wissing<sup>20</sup> state that an x-ray diagnosis of gallstone ileus has been made only eleven times. In the present case a definite preoperative diagnosis was made prior to the first jejunotomy, but only a questionable shadow could be seen on the first plate before the second operation. In an elderly patient who gives a history of previous gall-bladder disease, often with repeated episodes, the occurrence of a nonfulminating or recurrent obstructive syndrome, with perhaps a shifting focus of symptoms, suggests ileus caused by a gallstone. However, it is not particularly pertinent to the patient's welfare that an exact diagnosis of the nature of the obstruction be made. The important thing is to make a diagnosis of obstruction.

#### TREATMENT

Operation should be performed as soon as it is apparent that the progress of the stone has been arrested and that more or less complete obstruction of the bowel exists. In reviewing a great many case histories, one is struck by the number of patients who had mild obstructive symptoms, relieved by the passage of a stone or stones by anus. It is apparent that the vast majority suffered intestinal colic but not a frank obstruction, although the condition was reported as gallstone ileus. Such colic is set up partly by the obturating action of small stones, but also because of spasm due to irritation provoked by their passage. Wangenstein<sup>17</sup> mentions 2 patients with small stones and some degree of spastic obstruction who were treated with inlying duodenal tube suction, with later appearance of the gallstones in the stools. The distinction between intestinal colic and obstruction is well illustrated by the present case. The patient suffered colic with both defecated stones, but had no nausea, vomiting, distention or obstipation.

When a patient is having mild cramps, perhaps in varying locations, unaccompanied by vomiting and distention, he may be safely observed for a period during which bed rest, antispasmodics and a liquid diet can be instituted, while the abdomen is studied by x-ray and repeated examinations. In Murphy's<sup>24</sup> 125 cases, 70 passed the stone by anus.

However, immediate surgery is indicated if a diagnosis of intestinal obstruction is made. Suction decompression, as an adjunct to immediate surgery, is very useful. Its employment in lieu of immediate surgery, in the hope that a spastic obstruction may be relieved and the stone defecated, is a dangerous practice.

An enterotomy, without enterostomy or drainage of the abdomen, is the operation of choice. When possible the obstructing stone should be

milked upward a short distance, so that the opening in the bowel is not made at the point of incarceration, where wound-healing might logically be poor. The longitudinal incision may be closed transversely by an inverting type of suture, followed by a continuous Cushing stitch and completed by a series of interrupted mattress sutures.

Adhesions and kinking of the bowel may be minimized by tacking a free omental graft over the suture line with a few interrupted sutures. An enterostomy adds very definitely to the operative risk and is rarely necessary. Wangenstein mentions that it is occasionally possible to crush a stone within the lumen. However, Dulin and Peterson<sup>11</sup> report such an attempt in which the trauma to the bowel necessitated anastomosis between the ileum and cecum.

The possibility of multiple stones must be kept in mind at the time of operation. In 3 of Holz's<sup>9</sup> series of 5 cases of repeated operation for gallstone ileus, the second stone had to be removed during the immediate convalescence. It is probable that the second stone was already in the intestine at the time of the first operation. A great many surgeons<sup>19, 25-27</sup> have reported the finding of more than one stone within the intestine, often close together but occasionally separated by considerable distance. The presence of facets on the obstructing stone indicates the need for additional search, provided the patient's condition permits. Both the proximal intestine and the biliary tract should be palpated. The detection of stones within the gall bladder may be very difficult, owing to dense adhesions. Additional stones within the intestine can often be removed through a single incision. However, if a second stone is felt within the gall bladder, it is rarely feasible to remove it at the same operation, although Holz successfully removed the gall bladder and closed the cholecystoduodenal fistula after doing an enterotomy for the first stone. In the case reported here, the stone removed at the first operation had one facet which did not fit either of the two facets of the previously defecated stone, but it was assumed that a third stone lost by defecation was the explanation. However, this facet was later accounted for by the facets on a fourth, unexpected stone which had to be removed three months later, and which was presumably still in the gall bladder at the time of the first operation.

#### SUMMARY

A case of recurrent gallstone ileus is reported. Gallstone ileus occurs typically in elderly women with a previous history of chronic gall-bladder

disease. It is worthy of emphasis that this is an obturation type of obstruction.

The high mortality, 50 per cent, is chiefly the result of the advanced age of the patients and delay in operating on them. This delay is largely due to the variable, somewhat atypical obstructive symptoms.

Immediate surgery is imperative once the diagnosis of obstruction is made. However the patient may be given a reasonable chance to pass the stone by anus if the distinction between colic and obstruction can be made. Vomiting, obstipation, persistent colic, distention, hyperperistalsis and the typical appearance on the flat x-ray plate are features that indicate obstruction requiring surgery.

The stone may occasionally be visualized on x-ray examination.

The Miller-Abbott tube and 100 per cent oxygen inhalations appear to be valuable implements to surgery in such conditions, in addition to spinal anesthesia and the correction of fluid and chemical deficits.

An enterostomy is usually unnecessary. The possibility of multiple stones must be kept in mind at the time of the operation. It will rarely be desirable to carry out any surgical procedure in regard to the cholecystoenteric fistula.

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## REPORT ON MEDICAL PROGRESS

## ATHLETIC AND RELATED INJURIES

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REFERENCES to athletic trauma in the medical literature are relatively scarce, and the injuries are in many cases indexed under other diagnoses. Traumas produced by athletic activity, whether organized or recreational, are often similar to certain types of injuries received in industrial accidents. It would be a mistake not at least to mention some of the physiological aspects of muscular metabolism, as this field is important and as new developments are constantly appearing. Fractures as such will be considered only incidentally. In addition to the physiological aspects of muscular metabolism, this report will discuss the commoner types of injuries: sprains and strains of the extremities, injuries to the back, internal injuries and head injuries.

## PHYSIOLOGY OF MUSCULAR EXERCISE

Much interest in the physiology of muscular exercise has recently been manifested, but one still finds a relative scarcity of reference to the subject in the literature. Foster<sup>1</sup> has analyzed the direct effect of extreme physical exertion on the kidneys, and concludes that certain changes are apparent in the appearance of urine specimens before and after exercise. Abrahams<sup>2</sup> concludes that every test involving blood pressure in prolonged physical exertion is fallacious because of the emotional factor, and suggests that observation of the rate of cardiac deceleration would furnish a more satisfactory method. Similarly, Kellner,<sup>3</sup> having investigated the observations made by Faris, concludes that the excitement of examination does not cause any essential morphologic change in the white-cell count. And Nylin<sup>4</sup> demonstrates the practical applicability of the cardiopulmonary function test. But although these tests constitute attempts to standardize the measure of physical fitness, they have not yet been generally accepted as conclusive. The high blood pressure in an occasional young athlete is still an unexplained physiologic phenomenon.<sup>5</sup>

There appears to be little if any demonstrable basis for the claim that gelatin is valuable in combating fatigue. The conclusions of the Long Island College of Medicine report<sup>6</sup> are now be-

ing investigated by a series of experiments at the Harvard Fatigue Laboratory. However, the comment of the Council on Foods of the American Medical Association<sup>7</sup> seems of sufficient significance to bear quotation:

The experiments of Ray and his associates cannot be considered as conclusive. They represent uncontrolled observations, because no comparisons were made of the effect of feeding other proteins or other substances. Perhaps the chief point of criticism about the work performed is that the feeling of fatigue was the criterion for stopping work each day. It is well known that the mental factor in fatigue is enormous, and some method of controlling this factor could well have been included in the planning of the experiments. On the basis of available evidence the Council cannot recognize the claim that gelatin lessens or postpones fatigue.

## SPRAINS AND STRAINS

*Knee*

The literature on sprains and strains of the knee seems to be fairly full. In another place<sup>8</sup> have pointed out the large and increasing field of lesser but important trauma in sports and recreation and discussed the incidence of knee injuries in sports, with particular emphasis on the low incidence of internal derangements—less than 10 per cent of the 483 cases involved—attributable to treatment and especially to subsequent prophylactic treatment. Efskind<sup>9</sup> reports operations performed between 1928 and 1936 for injury to the semilunar cartilage in 36 patients, with all but 2 cases followed. In 13 cases the author observed diminution in the joint space where the cartilage had been removed and abnormal static changes in the articular cartilage, with no change in the knee not operated on. All but 20 of the patients returned to their regular work. Hopkins and Huston,<sup>10</sup> analyzing the end results of a series of 193 injuries to the knee out of a total of 259 major knee injuries sustained at Springfield College between 1924 and 1937, report that 89 per cent of the cases of simple synovitis and 81 per cent of those with a lateral ligament sprain showed good final results, all the patients being able to participate actively in athletics. The authors state that the results of semilunar cartilage injury treated by immobilization (46 per cent good) were suffi-

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ciently better than those treated merely by bandaging, rest, crutches and physiotherapy (36 per cent good) to warrant the use of a plaster cast as soon as a diagnosis had been made. They conclude "The results of conservative treatment are so satisfactory, nearly half being good, that we believe it should be tried in nearly all cases before resorting to operation. It is interesting to note that football was responsible for 90 cases (47 per cent), soccer for 24 (12 per cent), basketball and gymnasium for 16 (8 per cent) each, track for 10 (5 per cent), wrestling for 9 (5 per cent), baseball and lacrosse for 6 (3 per cent) each, and various other activities for 16 (8 per cent).

Milbourn,<sup>11</sup> in discussing 9 cases verified by operation, maintains that after injection of an opaque substance (Abrodil or Intron) the only roentgenological sign of concentric injury to the meniscus is that the triangular contrast defect at the site of the ruptured meniscus is much smaller than that of the other meniscus. He suggests that the sign of concentric meniscal injury generally occurs together with other signs in the arthrogram which indicate meniscal injuries.

Lambrinudi<sup>12</sup> reported to the Section of Orthopaedics of the Royal Society of Medicine 8 cases of injuries to both semilunar cartilages seen in two years, and stated that dual lesions of the semilunar cartilages occur more frequently than is realized, and ought to be suspected in all cases where the pain, associated with an injury to the external cartilage, is referred to the inner side. Dislocation of the external cartilage is more frequently associated with strain of the crucial ligaments than is the case with internal cartilages. The degree of ligamentous laxity and its symptoms were believed to be due more to slipping in and out of the external cartilage than to laxity itself; the author remarked that in such circumstances excision of the cartilage is a sound procedure.

#### *Shoulder and Upper Arm*

Gilcreest and Albi<sup>13</sup> have discussed the histology of injuries in the region of the deltoid muscle, citing the report and tabulation by Bunts<sup>14</sup> of 19 cases of isolated injury to the circumflex nerve, of which 8 were the result of dislocation and 7 of contusion. Clemens<sup>15</sup> report of a case of traumatic hernia of the deltoid muscle, Davis<sup>16</sup> report of a case of detachment of the deltoid from its bony origin, and the observations by Smith and Christensen<sup>17</sup> that no explanation of the mechanism of production of paralysis of the deltoid can be found in the literature, their report of 2 cases of paralysis following shoulder injuries, and their

conclusion that common shoulder injuries may result in a complete and permanent paralysis of the deltoid muscle. Gilcreest and Albi state that deltoid injuries must be repaired as soon as possible, and prescribe the wearing of an abduction splint at an angle of 90° in a slightly forward position for three or four weeks, with heat and gentle massage for about one week after the repair, followed by passive abduction of the shoulder by stooping exercises. They also recommend treatment ranging from the usual neuritis treatment to neurolysis or neurotomy for the restoration of the continuity of injured nerves and transplantation of the pectoralis and other plastic operations in cases of severe atrophy of the deltoid muscle. For rupture of the serratus magnus (anterior) muscle they state that if the nerve is involved early recognition of the extent of the lesion, the nutritional state of the paralyzed muscle and the extent of secondary changes in the antagonists are all factors in the prognosis, with surgical intervention indicated if the muscle cannot be stimulated to react to faradic or galvanic currents. They comment on 3 cases of subscapularis-muscle lesions and remark that no cases of this injury could be found in the literature. Also they could find in the literature no cases of rupture of the coracobrachialis muscle, but report 1 case, due to direct violence, in which an early operation resulted in complete recovery. In addition to the 10 cases of triceps muscle lesions found in the literature, Gilcreest and Albi report 3 cases, with the comment that early exploration and repair usually achieve a complete restoration. Attrition due to occupation, degenerative changes caused by senility, arthritis, myositis, arteriosclerosis, acute and chronic infectious diseases, fatigue and trauma are all cited as factors in rupture of the biceps muscle with early diagnosis and repair important in obtaining a complete restoration of function. Surgical repair is prescribed for elongation and dislocation of the tendon of the long head of the biceps muscle.

Kaplan<sup>18</sup> reports 5 cases of thrombosis of the axillary vein at Bellevue Hospital and recommends rest, elevation and hot moist packs applied locally with a hand-to-shoulder elastic bandage for residual edema. Excision of the thrombus or entire segment of thrombosed vein has been recommended by others, but Kaplan states that the advisability of such procedures is questionable.

#### *Wrist and Ankle*

Cave<sup>19</sup> discusses the pathology of fracture of the carpal navicular bone, its diagnosis and treatment and those who are interested should read

his article. The rare incidence of fractures of the carpus—approximately 2 per cent of all fractures, according to a review of 4500 cases at the Massachusetts General Hospital—is of interest. Woods<sup>9</sup> outlines the various types and treatment of fractures of the wrist and ankle. As a treatment for radiocarpal dislocations, he prescribes reduction by traction and immobilization in a standard cast for fourteen days, followed by strapping with a layer of plaster bandages reinforced by a few strips of Paragon Plaster with interlocking split tails. For inferior radioulnar dislocations, usually a complication of a severe Colles's fracture, Woods recommends reduction under anesthesia by pressure and manipulation, fixation for three or four weeks in a standard cast and strapping support until all symptoms have disappeared. He states that massage and passive movements are contraindicated for sprains of the wrist joint, the preferred treatment being immobilization in a non-padded dorsal splint of plaster of Paris for ten to twenty days. He recommends radiography for all dislocations of the ankle joint, because of the probability of associated fractures; treatment should consist of reduction under local or general anesthesia, followed by immobilization in a standard below-the-knee cast for ten days. For incomplete dislocation of the astragalus, reduction by traction and manipulation, with the knee flexed, followed by a plaster cast, are indicated, while for complete dislocation, screw traction or open operation when necessary, with astraglectomy and fixation in a plaster cast in extreme cases, is recommended. The author stresses the usually unfavorable prognosis in these injuries. Subastragaloid dislocation, whether posteromedial or posterolateral, requires prompt treatment with x-ray films of the foot and reduction under anesthesia, screw traction when necessary and a "walking" plaster cast for four to six weeks. According to Woods, the treatment of extra-articular sprains of the ankle—after x-ray examination has ruled out the possibility of fracture—should consist of a 5-cm strip of Paragon Plaster applied as a stirrup, a horizontal strip with its lower border level with the tip of the external malleolus, and with the tails of the strip wrapped alternately round the ankle, and daily massage for the leg muscles; the patient is directed to walk as naturally as possible. Application of Scott's ointment, massage, contrast baths (hot and cold) and radiant heat for severe cases are recommended for sprains with severe synovial involvement, with carefully selected and limited exercises.

Bunnell,<sup>21</sup> discussing the primary repair of severed tendons, states that such repair should be at-

tempted only under strict indications covering the nature of the wound and adequate surgical and hospital facilities. He recommends prompt operation, thorough debridement and the closing over of all vulnerable parts. The tendon suture should be simple and of non-irritating material, preferably stainless steel wire, and may be left in the tendon or placed in such a way that the wire is removable.

### *Hamstring Muscles*

Girard and Childress<sup>22</sup> report an injury to the hamstring muscle of the left thigh, sustained in football practice, and state that the formation of the fibrous tissue is inevitable in the repair of severe muscle tears, treated either conservatively or surgically. The resulting fibrous mass should be given consideration in its relation to adjacent nerves and vessels. Further efforts to repair the muscle in this particular case, the authors contend, would undoubtedly have produced additional scar tissue, with a recurrence of the nerve pressure symptoms. They observe that an excellent functional and cosmetic result has been obtained by complete excision of the semitendinosus muscle.

## INJURIES TO THE BACK

### *Lumbosacral and Sacroiliac Strain*

In a review of 150 cases, Gilcreest<sup>23</sup> attributes lumbosacral and sacroiliac strain to posture, trauma, infection, congenital anomalies and neurologic, metabolic and neoplastic conditions, with arthritis of no significance. He states that a very careful history and thorough examination are of the utmost importance in early diagnosis of this condition, in which roentgenograms are of little aid, and recommends early treatment by manipulation and a belt if necessary. Ten of the 150 cases were treated with a plaster-of-Paris body encasement. The majority of patients were in middle life, the youngest was nineteen and the oldest eighty, and the condition occurred oftenest in strong, robust, muscular individuals. Gilcreest comments on the difficulty presented by the frequent complaint of this condition among malingerers.

### *Rupture of the Intervertebral Disk*

An earlier progress report<sup>24</sup> has discussed rupture of the intervertebral disk and has pointed to the importance of an early neurological examination, accompanied by lumbar puncture in the treatment of patients with chronic back pain and pain referred to the lower extremities. Testing of the reflexes of the patients is a part of this examination.

## INTERNAL INJURIES

*Contusion of the Kidney*

Prather<sup>28</sup> discusses the pathological signs of contusion of the kidney, as well as the treatment, and points out that there was no evidence of shock in 90 per cent of the cases reported, that no fall of blood pressure was noticed during the first forty-eight hours of hospitalization and that no rise of increase in tenderness and spasm for the first forty-eight hours of hospitalization was apparent. A conservative, nonsurgical program was pursued. He also reports 8 cases of true rupture of the kidneys, with 4 successful operations and 2 deaths. Traumatic severance of the renal pedicle, he states invariably causes the death of the patient, but fortunately the condition is rare.

*Rupture of the Spleen*

Webb<sup>29</sup> expresses his belief that traumatic rupture of the spleen occurs more frequently than a review of the literature reveals, and emphasizes the necessity of bearing this condition in mind in all injuries to the splenic area and of keeping all suspected injuries under observation for at least fourteen days. Diagnosis is aided by a roentgenological examination and the treatment indicated is splenectomy. Webb cites a case of a successful splenectomy on an eight-year-old boy who was injured by a puck while watching a hockey game. Physiologic and pathologic conditions make conservative measures extremely hazardous, the author states, although spontaneous healing and recovery occasionally occur. Foster and Prey<sup>30</sup> have analyzed 20 cases of splenic rupture operated on in four Denver hospitals from 1927 to 1938. They state that correct diagnosis is not made frequently enough or early enough and give as two especially important diagnostic signs localized abdominal rigidity and shifting dullness. Preoperative transfusion and autotransfusion are often life-saving procedures but have not generally received proper recognition. The authors recommend splenectomy as the usual treatment with suture indicated only in cases with small lacerations due to gunshot or stab wounds. Tamponade should be resorted to only when any other type of surgery would undoubtedly cause death.

*Rupture of the Bladder*

Thompson<sup>31</sup> observes that traumatic rupture of the bladder, because of the increasing number of automobile accidents, is now being encountered oftener although the condition is still considered comparatively rare. A discouraging fact about such ruptures is the extremely high

mortality rate—about 80 per cent of both intraperitoneal and extraperitoneal types, two thirds of the cases being intraperitoneal. Surgical treatment is indicated and should be carried out as soon as possible. The author remarks that 90 per cent of such injuries occur in men, with alcoholism as a frequent contributing factor.

*Rupture of the Duodenum*

Among the more serious visceral injuries, traumatic rupture of the duodenum or of the retroperitoneal duodenum occurs very rarely but is usually fatal. Ottenheimer and Gilman<sup>32</sup> attribute the high mortality accompanying such ruptures to three factors: failure to make a diagnosis sufficiently early to render proper treatment effective; failure to recognize the condition at operation, and technical difficulties encountered in repairing the retroperitoneal duodenum and establishing adequate drainage of the retroperitoneal space. They observe that the discovery of gas in the retroperitoneal space, either preoperatively or at operation is almost pathognomonic of the condition and that radiographic films are indicated in all cases where a ruptured retroperitoneal duodenum is suspected.

*Traumatic Appendicitis*

Kessler<sup>33</sup> states that traumatic appendicitis rarely occurs, and that such a diagnosis should be accepted only when no symptoms or signs of appendicitis have existed before the accident and when severe injury of the abdomen or overexertion can be proved. An interval of two or three days without symptoms and full ability to work, he further observes, makes the asserted relation improbable.

Riedl<sup>34</sup> reports a case of an unusual injury sustained in football—a rupture of the gastrocolic ligament, with consequent peritoneal hemorrhage. A successful operation was performed, and was followed by recovery.

*Chest Injuries*

A recent study<sup>35</sup> demonstrates that spontaneous pneumothorax occurs more commonly than is generally supposed. The author of the study further states that this condition not only occurs in the apparently healthy but is usually characterized by an afebrile benign course with recovery in a few weeks. The incidence of the condition among college students is fairly high, 15 cases being reported in an average male student body of 2500. The causes may vary from laughing and coughing to straining and running but undue physical exertion is not necessarily a contributory factor. The treatment recommended is rest for at least a week after onset. It is perhaps pertinent to

remark that only 1 case of spontaneous pneumothorax—and that was caused by running—has been observed in organized athletics at Harvard University for the last eight years. Discussing the surgical treatment of chest injuries, Hegner<sup>33</sup> outlines the signs and symptoms, the treatment and the mortality rate accompanying such injuries, x-ray visualization is indicated after the patient has recovered from shock. Aspiration of as much blood as possible is recommended for all serious lung hemorrhages.

### HEAD INJURIES

An editorial in the *Journal of the American Medical Association*<sup>34</sup> mentions two dominating influences in the treatment of traumatic brain injuries in recent years: the demonstration of the four classic stages of brain compression by Kocher and Cushing, and the observation of Weed and his collaborators that increased intracranial tension can be influenced by changing the osmotic pressure of the blood by the giving of hypertonic or hypotonic solutions. Reports in recent years show that more attention is steadily being paid to differentiation in diagnosis of head injuries and to the effect of the treatment on the patient's life after recovery. Thus Schaller<sup>35</sup> differentiates between the post-traumatic concussion state and the post-traumatic psychoneurotic state. The former condition produces reversible changes of function of the brain, which in severe cases may become irreversible, the symptoms being headaches, vertigo, tinnitus, nervousness, impairment of memory and of vision, fatigability, poor concentration, sensitiveness to heat and intolerance to alcohol. The latter state, on the other hand, is characterized by fear, suggestion and wishful thinking, and is caused by the precipitation of psychic complexes, following a period of mediation in patients presenting inadequate personality traits and subjected to adverse mental influences. The author expresses the conviction that every post-traumatic neurotic person of the hysterical type is at least a subconscious simulator, while many are malingerers, and states that treatment must be prescribed with this fact in mind.

Another study of head injuries by King<sup>36</sup> places the patients in three categories: those who will recover with little treatment, those whose prognosis is uncertain and those who will probably die. Dehydration and lumbar puncture are recommended. The author considers lacerations of the scalp, depressed comminuted fractures of the skull vault, fissured fractures of the base and compound fissured fractures of the vault, and describes the treatment of these various injuries. The same

writer<sup>37</sup> states elsewhere that traumatic osteomyelitis is really not osteomyelitis but bone necrosis, caused by bone denudation in the presence of local infection. In another discussion of brain abscesses observed from 1920 to 1939, he<sup>38</sup> notes that 7 cases out of a total of 60 were of traumatic origin, and all were males between the ages of seven and fifty-four. All were operated on, and all made uneventful recoveries. These abscesses due to trauma, King points out, may be large or small, superficial or deep, they are usually irregular in shape and in 90 per cent of the cases are single. Preservation of life, removal of the pus with subsidence of brain edema and healing of the wound with recovery and return to normal life are cited as the main objectives of the procedure. Prompt removal of the cranial or extracranial source of infection is the operative procedure recommended.

With reference to the convalescent care of patients suffering from craniocerebral injuries, Munro<sup>39</sup> states that the convalescence should be planned so as to correlate the patient's needs with the injury and the resulting pathologic lesion, the preconvalescent period varying from seconds, in properly diagnosed cases, to years in neglected cases of subdural hematoma that have been incorrectly diagnosed as skull fracture. The convalescence begins after the patient has had a constantly normal intracranial pressure for two weeks, and must not only provide directions as to physical activity but embody in them enough applied psychology to prevent the patient from interfering with his own recovery. The convalescent care, moreover, should include plans to keep the associated destruction of initiative and self-confidence from developing into a permanent neurosis.

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It is interesting to note, in connection with injuries sustained in recreation, that in 1939 there were 13 deaths—5 fewer than in 1938—directly due to Fourth of July celebrations, and that cases of tetanus, burns and lacerations, loss of vision or injury to the eye, internal injuries, fractures, mutilations and other serious accidents were correspondingly fewer.<sup>40</sup> The reduction in the number of serious injuries from fireworks may be directly attributed to the effectiveness of more adequate legislation and general education of the lay public.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 26311

#### PRESENTATION OF CASE

A twelve-year-old boy, since the age of two years, had been observed and followed extensively in an outside hospital because of heart trouble. The birth history was not remarkable. The child received adequate vitamins and gained well during infancy, he had had bronchial pneumonia at the age of seven months, and since that time had experienced frequent colds, with noisy breathing. Physical examination at the age of two revealed a rather pale, under-developed infant with prominent frontal bossing. Examination of the heart showed marked enlargement to the left, a palpable systolic thrill over the precordium, and a loud, rough systolic murmur heard over the whole precordium and transmitted to the neck. Roentgenograms of the chest confirmed the cardiac enlargement, there also was evidence of diffuse pulmonary congestion. The child was seen on two occasions in the hospital's heart clinic, and at the age of three was treated in another department for acute cervical adenitis. Because of repeated colds tonsillectomy and adenoidectomy were done at the age of nine, he made an uneventful convalescence. The last visit to the same outside institution, three years before admission to this hospital, was for a routine observation of the patient's cardiac status.

On admission to this hospital it was learned that the patient had always complained of easy fatigability and slight dyspnea on exertion. He had a chronic cough, which had lasted for many years. About one week before admission his mother noted that ankle, scrotal and penile edema had developed. These symptoms slowly progressed, and four days before admission, while at breakfast, he suddenly complained of a severe substernal and epigastric non-radiating pain. His face and eyes allegedly became slightly swollen, and he began to vomit at recurrent intervals until the time of hospital entry. A local physician was called, who immediately gave him nine small green pills, one of which was taken every three hours. Because of emesis, however, he was unable to retain most of them. The urine had be-

come highly colored for the two weeks' interval before admission, and its amount had decreased markedly. The facies had been flushed, and he was forced to sleep on two pillows. No chills, fever, diarrhea, bloody urine, melena or hemoptysis was noted.

In the past he had experienced no childhood diseases such as measles, mumps, whooping cough, chicken pox, diphtheria or scarlet fever. Three siblings and the parents were living and well. The remaining family and past histories were non-contributory.

Physical examination revealed a fairly well-developed and well-nourished boy who appeared moderately ill but who was able to lie flat in bed comfortably, showing but slightly increased respirations. There was a little pitting edema of the lower legs, the scrotum and the sacrum. No clubbing of the fingers but a questionable clubbing of the toes was observed. The face, ears and fingers were flushed, and the eyelids and face appeared slightly edematous. The chest was somewhat enlarged on the left, and both lung bases were full of moist rales. The heart was markedly enlarged to percussion, being 3 cm. beyond the mid-clavicular line in the sixth interspace. In the fourth interspace the heart was enlarged 2 cm. beyond the mid-sternal line on the right. There was a precordial thrill with a to-and-fro, low pitched almost continuous murmur heard loudest over the fourth and fifth left interspaces, from which it was transmitted to the axilla and back. The apex beat was absolutely irregular at about 100 beats per minute, with a pulse deficit, the radial pulse being 60. The blood pressure was 108 systolic, 60 diastolic. The abdomen was scaphoid, the liver was palpated a fingerbreadth below the costal margin and was markedly tender, and there was a moderate amount of ascites. The remainder of the physical examination was negative.

The temperature was 96.4°F, the pulse at the wrist 55 (taken by a nurse), and the respirations 34.

Examination of the blood showed a red-cell count of 6,000,000 and a white-cell count of 17,000. The urine was negative.

The boy was restless, but not markedly uncomfortable. Shortly after admission he sat up and vomited bile, this seemed to relieve him, but a few minutes later he again attempted to regurgitate and fell backward on the bed. He was found to be pulseless, with slowly dilating pupils. He quickly failed, and died about two hours after admission to the hospital.

## DIFFERENTIAL DIAGNOSIS

DR. EDWARD F. BLAND. It seems to me that this case presents two fundamental problems. First, What were the structural abnormalities in this boy's heart? Second, Why did he die in the course of a week with the signs of acute heart failure, after having been in relatively good condition for twelve years? Ninety five per cent or more of children of this age in this section of the country who die of heart failure have rheumatic heart disease and active rheumatic fever and certainly one has to give serious consideration to the possibility that this boy had rheumatic heart disease. I think the evidence is against it but still we shall have to consider the possibility carefully. Certainly the type of heart failure which he exhibited at the end was consistent and fairly typical of this type of heart disease. The edema had the so-called nephritic distribution frequently seen with heart failure from any cause in childhood. We must assume that auricular fibrillation was present, although in the absence of graphic proof of it, I think we might register some doubt, especially since auricular fibrillation in childhood is relatively rare. We have seen it in patients as young as five years of age who had rheumatic heart disease, and once in an infant of three months with congenital heart disease. If auricular fibrillation is present in childhood it speaks a bit in favor of rheumatic heart disease, since it is even more rare with congenital heart disease. So much for the suggestive evidence of rheumatic disease in this case.

There are certain features which I think are rather strongly against this diagnosis. In the first place we have a record at the age of two that this boy had a cardiac thrill corresponding to a loud precordial systolic murmur. It usually requires a long time for a systolic thrill to develop in a rheumatic heart, and such a finding would certainly be most unusual at the age of two. After all, a thrill with acquired heart disease is dependent on a stenotic valve. However it is not uncommon at the age of two when associated with a congenitally defective heart. The absence of a rheumatic history is further slight evidence against a rheumatic background. I am inclined to think that he did not have rheumatic heart disease and that he did not die of rheumatic fever.

The second possibility that needs some consideration but is, I think, most unlikely is diffuse pulmonary arterial disease. There have been two such cases in children that I recall in this hospital one of which had a murmur similar in some respects to the description of the murmur here at the later examination, because of this murmur

the diagnosis of congenital heart disease was made. At postmortem the case proved to be one of pulmonary artery disease with thrombosis in the large vessels marked dilatation of the pulmonary arteries and probably functional regurgitation. The second case had no murmurs in the heart but the patient died at the age of ten after two years of a slowly progressive downhill course with right-sided failure. In the present case, again the observation at the age of two excluded the possibility that the physical signs in the heart could have been related to pulmonary artery disease. It takes years for serious heart failure to develop and even longer for the physical signs of such to appear. I do not believe we need seriously consider tumor of the heart or pericardium.

We are left then with the most likely possibility a congenital defect of the heart or great vessels—perhaps a combination of defects. There are a number of them which are consistent with a fairly normal life and with good functional reserve. I think we can accept the fact that he was not cyanotic. We have no real suggestion of it—only a red-cell count of 6 000 000. He had been vomiting and had congestive failure, and so might have been entitled to a single elevated red-cell count. Furthermore, the clubbing was questionable, and if questionable we had better discard it. The absence of cyanosis eliminates many of the more serious defects. We are left with two or three likely possibilities. The first and most probable is patency of the ductus arteriosus. We know that in some cases the physical signs of such may not be present at birth as presumably they were not here, but appeared somewhat later and were noted at the age of two. We also know that patency of the ductus may not be associated early in life with a continuous murmur usually it is, but it need not be. There is one finding that makes me hesitate a little, that is the enlargement of the heart from the time of the first observation. Ordinarily a patent ductus is very well borne, usually without serious enlargement of either ventricle. In a few unusual cases, for example the six or seven cases that have been operated on in other hospitals in Boston there is enlargement of the heart of considerable degree. However all these had a largely patent ductus, with a diastolic pressure of 20 to 30, a Corrigan pulse and a pulsating hilar shadow due to a free reflux of blood from the aorta into the pulmonary artery. I am inclined to think that patent ductus arteriosus is the most likely diagnosis in this patient but I think that because of the considerable enlargement of the heart it may be complicated by some other defect. It would be very helpful if we had an x-ray film, but I presume

the child died too soon. It would help also if we had an electrocardiogram, but I suppose the same is true of that, so we have to rely on the physical signs.

I am still a little disturbed about the size of the heart. An early x-ray film is reported to have shown diffuse congestion of the lungs. I interpret that as prominent vascular shadows due to a reflux of blood back into the pulmonary circuit through the ductus, but it raises the possibility of septal defect between the auricles, much less likely between the ventricles. The former is quite common with a patent ductus. I think we must assume, however, that the predominant flow of blood was from the systemic to the pulmonary side, at least for the greater part of this boy's life.

What else could he have had? Coarctation of the aorta? The blood-pressure levels do not suggest it, and there is no other reason to suspect it. Sub-aortic stenosis is relatively rare, although we know three patients who we think have this anomaly. They have all the classic signs of aortic stenosis but with an aortic second sound of normal intensity. I think this boy did not have sub-aortic stenosis, certainly not as the chief lesion. I am relying heavily on the description of the murmur just before he died. I hope that has been accurately described, otherwise I shall be led hopelessly astray. Certainly it is not characteristic of acquired heart disease. A loud murmur, systolic in time, extending into diastole in the left mid-heart and upper heart region, is characteristic of a patent ductus. So much for the structural changes.

Of perhaps more fundamental importance is the second problem, namely, Why did this boy without previous symptoms of serious limitation quickly die in the course of a week with the symptoms and signs of congestive failure? Most children with congenital defects or rheumatic heart disease who succumb in childhood with congestive failure die of some infection. It may be obscure. In those with rheumatic fever, it is usually rheumatic infection. In those with congenital heart disease, it is usually bacterial infection in the heart or in the lungs (pneumonia). If bacterial infection of the ductus existed in this case we should expect the emboli, if there were emboli, to go to the lungs. There is one episode which might be explained in this manner—the sudden acute pain substernally and in the epigastrium four days before he died. That might, however, have been due to acute congestion of the liver. Somewhat against bacterial endarteritis is the fact that the boy had no fever, but after all this is only a single temperature record and it was taken

only a short time before he died. It is mentioned several times that he seemed sick and that his face was flushed, and I am inclined to think there must have been a superimposed infection in the heart or nearby. He probably had subacute or acute bacterial endocarditis. If we are correct in the structural defects perhaps the rales in his chest were as much the result of pulmonary emboli or infarction as they were that of congestive failure. It was noted he could lie flat without much discomfort. That does not help since it is characteristic of heart failure in children, which is predominantly of the right-sided type, and hence the lungs may escape serious congestion.

Did he have pericarditis to account for the painful episode? We have no real reason to suspect pericarditis. A friction rub was not heard, the sounds were not masked, and there is no particular reason why he should have had pericarditis. What else, other than infection, could cause this acute heart failure in a child? Acute hemorrhagic nephritis occasionally results in cardiac dilatation and failure, but there is no real reason to suspect it. Undoubtedly he was entitled to have concentrated urine on the basis of heart failure. I am inclined to think we are dealing here with congenital heart disease, probably with auricular fibrillation as the precipitating factor for the congestive failure, possibly with a combination of defects, among which at least one, and most likely the only important one, is patency of the ductus arteriosus, possibly with superimposed bacterial infection and infarction of the lung.

DR ELI C. ROMBERG: With the extremely tender liver, could there be a terminal tricuspid involvement, probably of rheumatic nature?

DR BLAND: I do not believe so. In all the postmortems in children with rheumatic heart disease that we have seen, if the tricuspid valve is involved, the mitral valve is involved in 100 per cent and the aortic valve in about 70 per cent. We have not yet seen rheumatic tricuspid disease as an isolated finding. I should think occasionally there might be an acute terminal tricuspid involvement, in the course of a septicemia, but I do not believe this child had rheumatic heart disease, either acute or chronic.

DR WYMAN RICHARDSON: Could you not say that this child had a terminal pulmonary embolus without assuming infection was present?

DR BLAND: As the cause of the terminal heart failure the last four days?

DR RICHARDSON: Yes.

DR BLAND: Possibly, but probably the heart failure was precipitated by the auricular fibrilla-

tion, that alone could have caused the acute congestion

DR. TRACY B. MALLORY Pulmonary embolus is much less common at the age of twelve than at fifty

DR. BLAND Pulmonary embolus in children usually occurs only as a reflux from bacterial endocarditis or the endarteritis of a patent ductus. Have you seen it in a child, presumably arising from the peripheral vessels?

DR. MALLORY I cannot remember such a case.

DR. RICHARDSON I was thinking of it coming from the auricle.

DR. BLAND Yes, it is possible if he had auricular fibrillation, and I suppose he did from the description, although the heart rate was relatively slow, possibly due to the nine green pills which he vomited. In a child as sick as this one was, the ventricular rate with auricular fibrillation is ordinarily fast, usually 140 or 150, and difficult to control even with large doses of digitalis. The fact that the child died abruptly need not disturb us particularly. Many children with congestive failure die abruptly.

DR. J. H. MEANS Might not a child with congenital heart disease develop rheumatic infection?

DR. BLAND Yes.

DR. MEANS Have you seen it?

DR. BLAND Yes, I have, but I found nothing in the description of the physical signs here that would suggest the combination. The mitral valve was not involved. In the absence of physical signs of mitral valve involvement I hesitate to make that diagnosis.

#### CLINICAL DIAGNOSES

Congenital heart disease.  
congestive failure.  
auricular fibrillation

#### DR. BLAND'S DIAGNOSES

congenital heart disease patent ductus arteriosus  
congestive heart failure (due to auricular fibrillation?)  
bacterial endarteritis?  
pulmonary infarction?

#### ANATOMICAL DIAGNOSES

congenital heart disease patent ductus arteriosus  
pulmonary atelectasis  
anasarca  
chronic passive congestion

#### PATHOLOGICAL DISCUSSION

DR. MALLORY The autopsy showed, as the single finding concerning the heart, a patent ductus arteriosus. The right ventricle was very markedly hypertrophied more so than is common with patent ductus arteriosus. There was generalized anasarca with fluid in the pericardium. There was a moderate amount of pulmonary collapse, no pulmonary embolus, and no evidence at autopsy of any acute infection so that we can only make a diagnosis of congestive heart failure. The character of the patent ductus was of some interest because now that Dr. Gross\* has shown that it can be successfully ligated, we are always in search of suitable cases. In many cases it is a sizable vessel 3 to 8 mm. in length long enough so that it is possible to ligate it doubly although not to divide it. Dr. Gross has never been able to divide one although he hopes to be able to some time. In this case there was no cord at all. The pulmonary artery and aorta were in contact with a simple hole between them. I think it would have been impossible to ligate this "duct."

DR. BLAND We have to assume that the terminal heart failure was secondary to the cardiac arrhythmia and tachycardia.

#### CASE 26312

##### PRESENTATION OF CASE

A sixty-four-year-old unmarried woman was admitted to the hospital complaining of dyspnea, with precordial chest pain on exertion.

The patient was well until approximately two years before admission when she began to notice an epigastric tightness which occurred following the ingestion of a large meal or following severe exertion. The tightness was described as a pressure sensation which radiated over the precordium and down the inner aspect of both arms to the wrists. It was relieved by rest as was also a slight but definitely increasing dyspnea with exertion. These symptoms persisted but she was able to work as a housekeeper until five weeks before admission when she suddenly developed a dull aching precordial chest pain with characteristic arm radiation, which persisted for at least twelve hours without being relieved by rest. Following this attack, breathlessness developed on climbing stairs. She consulted her physician, who prescribed nitroglycerin tablets, which she stated, relieved the attacks of epigastric and precordial tightness with arm pain, but failed to improve the dyspnea with exertion. She noticed an increasing easy fatigability with slight but definite malaise

\*Gross, R. E. Surgical approach for ligation of patent ductus arteriosus. *New Eng. J. Med.* 220:510-514, 1939.

and three weeks before entry gave up work. Two weeks before admission the breathlessness was so severe that she was unable to climb stairs, and one week before entry, while en route to visit her physician three blocks from home, she was forced to rest at least three times. She was digitalized by her doctor at this time, with a marked improvement so that she felt "well" and noted a marked decrease in dyspnea with effort. She had experienced no orthopnea, paroxysmal nocturnal dyspnea, ankle edema, cyanosis or other cardio-respiratory symptoms.

The patient had noticed yellow plaques about both eyes for practically her entire life. Similar plaques and yellow deposits elsewhere beneath the skin developed at an early age but she thought little of them, since her mother, her only sister and two of seven brothers had similar nodules. Two of the brothers and the sister had had symptoms of "angina" for years. The remaining family and past histories were non-contributory.

Physical examination revealed a slightly obese woman in no apparent distress. She lay flat in bed without dyspnea. The heart was normal in size, and its rate was 80, with normal rhythm, there were no murmurs. The blood pressure was 115 systolic, 75 diastolic. There were a few fine crepitant rales posteriorly at both lung bases. The abdominal and pelvic examinations were negative. There were large, bright yellow, slightly raised angular plaques about both eyelids. Similar but larger and less yellow nodules were present over both olecranon processes and tibial tuberosities, over the extensor tendons of the middle carpo-phalangeal joints, and over the middle phalanx of the third right finger. These nodules varied up to 3 cm. in diameter and appeared to be attached to the bony landmarks in their localities. The skin overlying them was smooth, apparently unattached and transmitted a faint yellow hue. The Achilles tendons were bilaterally enlarged, and yellowish deposits were present in both of them. The remaining physical examination was negative.

Examination of the blood showed a red-cell count of 4,800,000 with 100 per cent hemoglobin, and a white-cell count of 5600 with 64 per cent polymorphonuclears, a smear was normal. The urine examination was negative. The blood Hinton test was negative. The blood cholesterol was 285 mg per 100 cc. An electrocardiogram showed a normal rhythm and a rate of 80, with blurring and widening of the QRS complexes, which equaled 0.10 second in duration, there was left-axis deviation, with diphasic T<sub>1</sub>, flat T<sub>2</sub>, upright

T<sub>3</sub> and small R<sub>4</sub>. Two other electrocardiographic tracings showed essentially similar findings.

Roentgenograms of the chest showed that the heart was enlarged in the region of the left ventricle, where it was more rounded than usual. The transverse diameter of the heart was 16.2 cm., while that of the chest was 26.5 cm. There was a little fluid in the left pleural cavity, and by fluoroscopy a smaller amount of fluid was noted in the right pleural cavity. The pulmonary vessels appeared slightly wider than usual. There was calcification of the somewhat tortuous aorta. Films of the hands showed soft-tissue swelling in the middle phalanx of the right fourth finger. Several of the interphalangeal joints showed small subcartilaginous defects. There was another soft tissue swelling lateral to the base of the right fifth metatarsal. The knee joints showed evidence of deforming arthritis. Anteroposterior views of the elbow joints showed no evidence of disease.

The patient remained in the hospital for eleven days, during which time the temperature, pulse and respirations remained normal. She felt well and could not understand why she was being hospitalized. On the eleventh hospital day, however, at 7:30 p.m. she suddenly gasped, became comatose, developed stertorous breathing and showed a patchy cyanosis, and died within a few minutes. It was observed that the heart ceased beating before the patient stopped breathing.

#### DIFFERENTIAL DIAGNOSIS

DR EARLE M. CHAPMAN. We are presented with a patient who seems to have died of heart disease, and from the history it sounds as if the patient had had attacks of angina, and that members of her family had angina. In trying to analyze the situation the most significant thing to me is that there was a familial tendency manifested by the patient and others of her relatives not to metabolize cholesterol properly. This family history is very interesting. Knowing that she had had yellow plaques on the skin since a very early age, one guesses immediately that these plaques contained a good deal of cholesterol, that the ones on her eyes were more or less typical so-called "xanthelasma" and that the remainder would be classified as xanthomas (xanthoma tuberosa). I think the x-ray description of the attachment to the periosteum is typical of that condition. There is no mention of neurologic changes, but of course we know they can occur with xanthoma tuberosa. This failure to metabolize cholesterol must have been a factor also in the development of the heart disease.

Why did she metabolize cholesterol improperly? I do not know. She apparently had not suffered from gall-bladder disease, since there is no history of a past attack of gall-bladder colic. We do know that the blood cholesterol was 285 mg per 100 cc.—the normal range is 150 to 230 mg. Such a definite elevation is oftentimes associated with a low basal metabolic rate, but unfortunately there is no record of the latter. Was it determined?

DR. TRACY B. MALLORY: No.

DR. CHAPMAN: What are the structural possibilities of the heart disease that was present? It seems to me that she probably had plaques of cholesterol similar to those shown on the external surfaces of the body, located in the coronary arteries. She had had one attack, if you will remember, five weeks before admission when she suddenly developed a dull aching precordial chest pain with characteristic arm radiation; this persisted for at least twelve hours. The duration of the attack suggests that there might have been a thrombosis or occlusion of the artery, with the formation of a myocardial infarct, at that time. Apparently the course was progressively downward from that point, because it was after this that she consulted a physician and received digitalis, and she died five weeks afterward.

The x-ray findings raise certain questions. Did the plaques of atheroma involve the aortic valve? In other words, did this woman also have calcific aortic stenosis? There is nothing in the physical examination to suggest that. We notice that the heart was normal in size. There were no murmurs. It does not comment whether the aortic second sound was loud, diminished or absent, an observation that might have helped in determining the presence of calcific disease in the aortic valve.

DR. JAMES R. LINGLEY: The film of the chest shows enlargement of the heart chiefly in the region of the left ventricle. There is calcification in the aortic arch but no note is made in the record regarding calcification in the aortic valve and it need not show in a film of this quality. The diagnosis must be made by fluoroscopy and confirmed by appropriate films. The films of the hands show this soft-tissue mass on the dorsal aspect of the finger. It is interesting that the density of the mass is the same as that of muscle and that it is not the density of fat.

DR. CHAPMAN: It says that there were subcartilaginous defects.

DR. LINGLEY: The bones of the hands show calcification and these areas of erosion close to the joints.

DR. CHAPMAN: You do not see anything in the bones of the skull. Xanthomatosis has been associated with the Schüller-Christian syndrome, but I think we can exclude the latter by these skull films.

DR. LINGLEY: In the Schüller-Christian syndrome there are large, round or oval, sharply defined areas of destruction in the skull. The skull in this case appears normal.

DR. CHAPMAN: The report says that there was a small amount of fluid in the left pleural cavity and by fluoroscopy a small amount in the right pleural cavity. Do you think there was any fluid in the pericardium?

DR. LINGLEY: No.

DR. CHAPMAN: A case of pericardial effusion supposedly due to the presence of cholesterol crystals was reported<sup>1</sup> two years ago in the *American Heart Journal*. Cholesterol crystals were recovered from the pericardial fluid. It occurred to me that that might be the case here, but it seems unlikely.

The electrocardiogram showed evidence of coronary disease, and we know too, that the patient had received digitalis before entry. These changes probably are not entirely typical of a digitalis effect. To me they are more suggestive of some interference with the conduction system. Widening of the QRS complex and a flat T<sub>s</sub> suggest coronary occlusion.

In trying to summarize the whole situation it seems likely that the patient had a disturbance of cholesterol metabolism. She had plaques of atheroma, and it is possible that she had one in the coronary artery which five weeks before entry following spasm of the artery led to a small infarction of the heart. The findings on entry are consistent with that. Because the heart muscle was able to re-establish itself, she seemed well in the hospital until the terminal episode, when she turned over in bed and died. The artery again went into spasm, and I do not see how we can say that she had a fresh thrombus and a fresh infarct. I think it was spasm due to the old focus five weeks before and that a fresh thrombus and a fresh infarct were not revealed at autopsy. I do not see how we can consider pulmonary infarction or perforation of the heart wall from the old infarction as the cause of death. I think she would have cried out in pain if she had ruptured the heart at the last moment. This process must have involved the conduction system of the heart.

It is interesting that the role of cholesterol in causing arteriosclerosis was not clearly pointed out until the work of Hueck,<sup>2</sup> in 1920 and that of Amitschkow<sup>3</sup> in 1925 showed that typical changes

in the vessels could be produced in animals by dietary means. One must have cholesterol present in the diet in order to produce these atheromatous changes as the other lipoids will not cause experimental atheroma. I should have been interested to know what the fundi showed, because certain types of changes occur in the eyes that we now think are associated with this disturbance in cholesterol metabolism.

DR MALLORY: Have you any comment on the electrocardiogram, Dr Bland?

DR EDWARD F BLAND: Three were taken during the stay in the hospital, and all are abnormal. The T-wave changes are probably a digitalis effect. The QRS complexes are a little slurred and suggest coronary disease, but on surveying the three I note no progressive changes and hence from these alone cannot make a final diagnosis of myocardial infarction.

I recall, but cannot remember the details of the article, a report by a Swedish observer<sup>4</sup> in the *Archives of Internal Medicine* a year ago in which the histories of some seventeen families were given, pointing out a premature appearance of heart disease of the coronary type in people who showed high blood-cholesterol levels and diffuse deposits of xanthoma over the body, some of which were in the heart and internal organs. This case sounds to me very much like the condition that he described, except that he was struck by the premature appearance of coronary disease. I wonder if this case may not be closely related to or perhaps the same as these.

DR WYMAN RICHARDSON: I should say this patient did quite well. If I live to sixty-four without coronary heart disease I shall be rather proud.

#### CLINICAL DIAGNOSES

Arteriosclerotic heart disease  
Xanthomatosis  
Coronary thrombosis, acute, recent

#### DR CHAPMAN'S DIAGNOSES

Disturbance of cholesterol metabolism, familial  
Xanthomatosis  
Atheromatous heart disease, with coronary occlusion and myocardial infarction (five weeks old)

#### ANATOMICAL DIAGNOSES

Xanthomatosis  
Arteriosclerosis  
Coronary thrombosis with infarction of the heart  
Chronic passive congestion

#### PATHOLOGICAL DISCUSSION

DR MALLORY: The postmortem examination showed severe coronary disease, both old and relatively fresh. The main branch of the left coronary artery was reduplicated, one of its branches being completely stenosed with old calcific material, the other was occluded with a fairly fresh, but partially organized, thrombus, quite consistent with five weeks' duration. The left ventricle showed an aneurysmal dilatation, part of which projected anteriorly. The major part of it was in the region of the interventricular septum and projected into the right ventricle, the x-ray had no chance of showing it, since it was in the wrong plane. It was a true intracardiac aneurysm, the sac bulging from one chamber into another chamber of the heart. The other coronary branches were markedly atherosclerotic, as was the aorta. There were several rather large plaques of atheroma in the pulmonary artery, rather more than is usual at the age of sixty-four. I am not able to say, however, that either in the systemic or the pulmonary circulation this atheroma was any more extensive than that which one commonly sees in an individual of this age. As regards the rest of the body, there were very extensive atheromatous deposits in many tendons and in numerous areas of the subcutaneous tissue, as we learned from the physical examination. There were no extravascular deposits within the internal organs.

This disease, if it is a disease, or group of diseases called primary xanthomatosis appears in a number of different forms, and in one of the very characteristic types it is associated with jaundice and with extensive cholesterol deposits in the liver and sometimes in the bile ducts. These were not present here. There were two small yellow nodules in the gall bladder, but very small ones. The other findings were of no particular interest, the ordinary effect of prolonged congestive heart failure.

DR CHAPMAN: Were the plaques in the coronary artery of this peculiar bright-yellow tint described here?

DR MALLORY: They were not obviously different from any ordinary atheromatous plaques.

DR CHAPMAN: Were there no cholesterol studies?

DR MALLORY: A great deal of material was taken by the Arthritic Service for chemical study, as yet I do not know the results. I think this is the first case of this disease that has been autopsied at this hospital. It is not particularly rare,

however, a familial history is quite characteristic if one looks for it.

DR. RICHARDSON I should think this case would be an argument against the theory that a high blood-cholesterol level produces coronary disease, because if it were cholesterol that produces these lesions that she had had since childhood it should be the very case that would have had coronary disease at the age of twenty or thirty.

DR. MALLORY In the paper that Dr Bland

mentions a number of families were reported in which the average age of onset of coronary disease was significantly low.

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# The New England Journal of Medicine

Formerly the  
Boston Medical and Surgical Journal  
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND  
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE  
ON PUBLICATIONS

Official Organ of  
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MATERIAL for early publication should be received not later than noon on Saturday.

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## THE CHILD-REFUGEE PROBLEM

THE American people have always been noted for their individual generosity and for the spontaneity of their response when aid has been sought for those in trouble. Naturally, this response is elicited most particularly when the disaster is overwhelming, when the need is urgent, and when the circumstances are dramatic. We require only an appeal that stirs our emotions, and our hearts are opened, our purse strings loosened. As a nation that tries to be business-like we are Uncle Shylock, as a group of individuals we heed the first call for help.

Today we are touched as never before, for it is not an act of Nature that has brought tribulation to many millions of people. No earthquake has devastated a community, no river has risen

beyond its banks, no hurricane has torn through a populated countryside. This time red-handed man has turned against his neighbors, and home and hearth and family are swept into the area of total war. The appeal is particularly pathetic. The children of a kindred nation are being exposed to the hazards of mechanized barbarianism, and we are asked to save them and to shelter them until they can be returned in peace to their families and homes, if families and homes remain.

Speed would seem to be of the essence, and yet the pitfalls for such a crusade are many if plans are not carefully laid and the emotionalism that governs our actions is not transformed into a calculated activity. We must remember, when we open our hearts and sweep our hearths to receive these English children who have been deprived of the privilege of security, that we can more than match their numbers with underprivileged children in our own communities whose less effectively voiced appeals have never, perhaps, reached our ears. We must remember that the foreign child for whom a well-intentioned agency requires from us a comfortable minimum of support and education may, on the expiration of the war, return to a home—like many of our own homes—for whose hardships we have ill adapted him.

The safety, the well-being, the education of our youthful hostages of fate should be provided for on a scale commensurate with the environment from which they come, but too much sentimentality will interfere with the expeditious transaction of the business. The foster parents, also, must be protected from too severe a repercussion of their generosity. If those who are answering the appeal of this good work are to guarantee subsistence to an unknown waif, they must have some guarantee that mistakes in matching the child to the home are also to be rectified. The best committee under these circumstances is one that accepts continuing responsibility.

Let us be willing—and we are willing—to give these bewildered refugees equal advantages with our own children of an equal economic station,

but let us not forget, in the exaltation of our emotionalism, that we have not borne our own less dramatic burden too generously in the past

## ALIENS AND THE PRACTICE OF MEDICINE

THE RECENT rapid influx of refugees to the United States has brought to the front some problems which are relatively new. Immigration in the past has chiefly involved the assimilation of workers in the lower grades however as of June 30, 1939, a total of 4549 refugee physicians had entered the United States in nine years, 1385 arriving within the previous fiscal year.\* It is usually thought that under the present system of giving medical care, there are already too many doctors in the United States, and just how medical practice can be provided for the newcomers from abroad is not clear. Is it to be by taking practice and therefore livelihood from members of the American medical profession so that more of them are to become unable to support themselves? Fear has been expressed that further overcrowding will lead to further degradation of medical practice.

Methods of restriction have been rather widely adopted by the states and fall into three groups: those requiring citizenship (declaration of intention or full citizenship), those requiring supplementary educational experience and those requiring fulfillment of conditions that are almost or quite impossible for the refugee to meet. While these restrictions have been advocated on the ground of protection for the public, their relation to protection is not always clear. The insistence on citizenship for the physician suggests the nationalistic spirit and unbridled nationalism has wrought such havoc, at least in the past half century that we may well question such an attitude to see if it be for good or ill.

Although the science of medicine and the art of scientific medical practice ought to be the same the world over, if two groups of people have lived in comparative isolation they may have customs

and conventions differing in many important respects, even if both groups are relatively highly civilized. Thus there is, on occasion, some reasonable basis for the requirement made by a few states that the foreigner spend one year in an approved medical school in the United States and another year in an approved hospital as intern before he is admitted to examination for registration. But how absurd these requirements are in the case of some distinguished specialist from abroad, if the candidate is expected to learn merely more medicine!

Requirements which are almost or quite impossible for the candidate to meet deserve careful scrutiny. Is their imposition because they are a restriction merely a manifestation of benighted nationalism? Or has it been shown clearly that there are too many well-equipped physicians for the good of the public, so that the protection of the public demands a numerical restriction? Are these requirements other or more difficult to fulfill for foreigners than for persons who have received their medical education in the United States? The apparent justice of having the same or similar requirements for all candidates deserves thoughtful consideration. What is the justice in removing restrictions so that it is easier for a foreigner to become registered as a physician than it is for a native? There are a number of problems here which do not seem to have received sufficient attention.

What is the justification for the requirement of citizenship, or of declaration of intention leading ultimately to citizenship? Is the alien, because he is an alien a better or a worse doctor than is a citizen? Of course the answer is that he is no better and no worse, as such. Yet a person living all his life according to one set of customs can undoubtedly continue in their observance more easily than can another person who is precipitated into their midst after fifty years in quite different surroundings.

The importance of the differences of custom and convention is quantitative. If there were some test of the amount of adjustment attained in one or two or five years of residence that might be a

\*Editorial Citizenship condition precedent to medical licensure to the United States. J. A. M. 4 113:1496, 1939

reasonable, though possibly difficult, procedure to apply. But citizenship is no measure of actual adjustment or of actual competence at any stage in the procedure, and laws demanding it as a prerequisite to licensure appear to be the result of a possibly well-intentioned but probably misdirected effort to protect doctors and, perhaps through them, the public. From some points of view, though not all, it may be regarded as questionable statesmanship.

There is another way of regarding citizenship, namely, as a great privilege carrying with it real advantages—a great opportunity to exercise the power which belongs to adulthood, instead of restricting oneself to political infancy or childhood. If these are the things citizenship represents, aliens might well be eager to secure them.

## MEDICAL EPONYM

### COLLES' FRACTURE

In the *Edinburgh Medical and Surgical Journal* (10 182–186, 1814) appears a communication "On the Fracture of the Carpal Extremity of the Radius" by Abraham Colles (1773–1843), Dublin physician, one of the professors of anatomy and surgery in the Royal College of Surgeons in Ireland.

The injury to which I wish to direct the attention of surgeons, has not, as far as I know, been described by any author.

This fracture takes place at about an inch and a half above the carpal extremity of the radius, and exhibits the following appearances:

The posterior surface of the limb presents a considerable deformity, for a depression is seen in the forearm about an inch and a half above the end of this bone, while a considerable swelling occupies the wrist and metacarpus. Indeed, the carpus and base of metacarpus appear to be thrown backward so much, as on first view to excite a suspicion that the carpus has been dislocated forward.

On viewing the anterior surface of the limb, we observe a considerable fulness, as if caused by the flexor tendons being thrown forwards. This fulness extends upwards to about one third of the length of the forearm, and terminates below at the upper edge of the annular ligament of the wrist. The extremity of the ulna is seen projecting towards the palm and inner edge of the limb, the degree, however, in which this projection takes place, is different in different instances.

R W B

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#### FATAL DOUBLE PNEUMONIA IN PREGNANCY

Mrs. A. K., a twenty-three-year-old primipara, entered the hospital on March 19, 1939, with a diagnosis of pneumonia. She was in the thirty-first week of pregnancy.

The patient's past and family histories were negative. Catamenia began at twelve, were regular with a twenty-eight-day cycle and lasted four days. The last period began on August 15, 1938, making the expected date of confinement May 22.

The patient was first seen in the third month of pregnancy. An examination at that time was normal in every respect. The pregnancy progressed normally and uneventfully until March 18, when she was seen by her physician. She had had a head cold for a week, and had developed a cough and general soreness and pain throughout the body. She also complained of a headache. The temperature was 101°F., and the pulse 100. The following day she was sent to the hospital.

On admission the patient was cyanotic, respirations were labored and wheezy. The temperature was 103.6°F., the pulse 120, and the respirations 45. The eyes, ears, nose and throat were negative. Rales were heard throughout both lungs, both back and front. There was dullness in the right lower lobe. The heart was within normal limits, there were no murmurs. The abdomen was distended and showed a mass the size of a seven months' pregnancy. The white cell count was 15,900. The sputum was sent to the laboratory for typing. Narcotics were given for pain.

On the following day, March 20, the white-cell count was 3500. A consultant's notes read: "The woman is markedly cyanotic, with labored and rapid breathing. The radial pulse is very small in volume, and the heart rate rapid. The lungs on both sides are filled up, as evidenced by numerous moist rales. In addition there is extensive bronchial breathing all over the left back, with some on the right. My impression is that she is

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

overwhelmed with pneumonia, and I doubt if any form of treatment will be of avail. If the general condition should improve, even without being able to determine the type of pneumonia, I think it would be worthwhile to try sulfapyridine. Cultures of the blood and sputum were reported as containing *Staphylococcus aureus*. The patient grew steadily worse and expired at 1:15 p.m. on March 20, undelivered.

An autopsy, in which no organs were removed, showed the following: bronchopneumonia, right lower lobe, and confluent pneumonia, left lower lobe (*S. aureus*), multiple abscesses, right lower lobe, acute fibrinous pleuritis on the right, pyothorax on the right, acute passive congestion of liver, pregnancy, approximately seven months.

**Comment.** This case illustrates the value of taking care of any upper respiratory infection during pregnancy. Apparently the patient did not seek medical advice until she was quite sick. Had she been put to bed at the beginning of the infection, it is barely possible that pneumonia might have been averted. The disease was of the extremely fulminating influenzal type, with a superimposed *S. aureus* infection. When the patient arrived at the hospital, it is interesting that the medical consultant made the statement, "If the general condition should improve, I think it would be worthwhile to try sulfapyridine." Apparently she was so sick on admission that the outcome was considered hopeless. The patient died undelivered. The seriousness of pneumonia during pregnancy cannot be disregarded.

## DEATHS

**CLARK**—J. PAYSON CLARK, M.D., of Boston, died July 21. He was in his eighty-first year.

Born in St. Louis of Virginian ancestry, he came to Boston in his youth, attended Roxbury Latin School and Harvard University and received his medical degree from Harvard Medical School in 1887. He was house officer at the Massachusetts General Hospital and the Boston Lunatic Asylum. Following further study in Vienna and Dublin, he began his practice in Boston.

Dr. Clark was a member of the Massachusetts Medical Society and the American Medical Association, a fellow of the American Laryngological Association of which he had been treasurer and president, and a member of the American College of Surgeons.

A sister survives him.

**HOOPER**—GEORGE H. HOOPER, M.D., of Belmont, died July 24. He was in his forty-ninth year.

Born in Champion, Michigan, he attended Lawrence College, Wisconsin, and Tufts College Medical School, where he received his degree in 1919. He served his internship at the Boston City Hospital.

Dr. Hooper was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

**MULDOON**—MARY T. MULDOON, M.D., of Lexington, died July 18. She was in her forty-seventh year.

Born in Boston, she received her degree from Tufts College Medical School in 1915. For the last twenty years she had been connected with the Fernald School.

Dr. Muldoon was a member of the Massachusetts Medical Society and the American Medical Association.

A sister and niece and nephews survive her.

**WHORISKEY**—JOHN J. WHORISKEY, M.D., of Cambridge, died July 26. He was in his sixty-fourth year.

Born in Cambridge, he received his medical degree from Harvard Medical School in 1899 and served his internship at St. Elizabeth's Hospital, where he was chief of staff for many years.

Dr. Whoriskey was a fellow of the Massachusetts Medical Society and of the American Medical Association.

His widow and three sons survive him.

## MISCELLANY

### NOTE

The appointment of Dr. John W. Chamberlain, of Belmont, as assistant director of the Department of Hygiene at Massachusetts Institute of Technology was recently announced. Announcement was also made of the appointment of Dr. Robert T. Monroe and Dr. Edward Harding, both of Brookline, as assistants to the director, Dr. George W. Morse. Dr. Chamberlain, who has been an assistant in the Department of Hygiene since 1937, will share with Dr. Morse the administrative duties of the department, including supervision of the Homberg Memorial Infirmary, which cares for the health of 3000 students.

## CORRESPONDENCE

### A EUROPEAN EXPERIENCE

*To the Editor.* These notes cover the period when I was a George Gorham Peters Traveling Fellow in Surgery between January and May 1940. The greater part of the time was spent in the Department of Surgery of Edinburgh University and on the wards of the Royal Infirmary, Edinburgh, under the direction of Professor J. R. Learmonth.

I had planned to go to Europe in September 1939, but, with the onset of war, my trip was canceled. However, as winter came on and hostilities on the western front did not increase, it seemed worthwhile to go ahead with my original plans. So I sailed from New York City on December 30, 1939, on the *S.S. Manhattan* for Genoa, Italy, and had a calm, uneventful trip until we reached Gibraltar six days later.

Gibraltar harbor was full of activity, with armed British vessels constantly coming in and out of the harbor and numerous ships standing by waiting to be inspected for contraband by the British authorities. The *Manhattan* dropped anchor to wait its turn and since it was to remain in port for forty-eight hours the passengers were allowed shore leave. An air raid warning was sounded while I was ashore, which sent everyone scurrying for shelter, but it proved to be a false alarm. Nevertheless, it offered a proper introduction to present-day Europe. The hills of Spanish Morocco just about seven miles across the Straits of Gibraltar were clearly visible and were said to be heavily fortified. However, although only a few of the fortifications could be seen, I was struck by the apparent impenetrability of the Rock of Gibraltar.

The *Manhattan* docked in Genoa on January 9. There I remained overnight in order to do some hurried sight-seeing and then caught the Rome-Paris express on January 10. Soldiers in uniform were to be seen everywhere, but at that time there was no noticeable warlike tension.

Paris, where I arrived the following morning, was dark, gloomy and sandbagged. There was a definite sense of war in the air, and no trace of the traditional Parisian gaiety. The railroad stations were teeming with troops coming and going. In fact, it seemed to me that nine out of every ten men in the city were in uniform, either in the dress of the regular army or of one of the colonial troops. My twenty-four hours in Paris instead of being gay were quite depressing, due in part to the French blackout—my first—and the dim, cold blue lights permitted on the streets.

On January 12 I set off to Calais to cross the channel to England. The channel crossing was made on a small boat convoyed by several destroyers. About midway across the channel we passed a large spot of oil and debris where it was pointed out that a tanker had struck a mine the day before. The life belts which both passengers and crew were required to wear throughout the trip, at first clumsy and uncomfortable, seemed most reassuring. There were very few civilians on board but a good many British soldiers. Instead of Dover, the regular pre-war terminal for the run from Calais, the boat docked at Folkestone, for Dover was said to be a vital part of the military life line between Britain and France and hence closed to civilian traffic. Here at Folkestone the customs and passport inspection was strict, whereas in France and Italy it had been rather lax. I went directly to London and arrived during a blackout and a fog. There is nothing darker than this combination. It was not an encouraging outlook for a visitor, so on I went to Edinburgh where I arrived just fifteen days after leaving America.

I arrived in Edinburgh also during a blackout, and it seemed to me, if possible, to be even darker than it had been in London. Automobiles had only one headlight which cast a beam of light about ten yards, and the street-cars had very dim running lights. The first few nights I found it difficult to get around in the blackout, but one quickly becomes adjusted. To be sure, people went out at night much less than in normal times. When one did go out after dark, a small flashlight was essential, but it was absolutely taboo to shine a flashlight skyward. I found flashlights and batteries expensive and scarce, so my pocket examining light did double duty and became a treasure for after-dark walking. Daylight saving, instituted in March, was a great help. Interestingly enough, there was no increase in crime with the institution of the blackout, although road accidents were frequent during blackout hours for obvious reasons. To me these hours of enforced darkness, while serving as a defensive measure, were a constant reminder of the war.

Since my days were to be spent largely in the Royal Infirmary, I was fortunate to obtain a comfortable room in a house nearby. The landlady was a delightful elderly Irish woman, who made the best of everything, including food rationing and hard times. At mealtimes I met the other lodgers—an army officer, a secretary, an insurance man and a fifth year medical student—and with them talked war, for that was the main topic of conversation in the house at all times. Their attitude throughout was one of determination, but they, like everyone, were depressed. This outlook of depression was reflected in the appearance of the town in general. There were no flags flying or bands playing, soldiers were everywhere, not in brilliant parade uniforms, but in the somber garb of battle dress.

Food rationing was of great interest to me. It was not in effect for actual shortage of foodstuffs but in anticipation of the months ahead. In each city there were one or more food-control offices where ration coupon books were obtainable. According to custom these were given to the landlady, who did all the shopping, but it was not necessary for persons in transit to present a ration book to eat at hotels and restaurants. Food was rationed by price more than by individual needs, and in the *Lancet* (1743, 1940) there was an excellent common sense discussion of the problem. There it was pointed out that people in the low income groups are pushed farther away from an adequate diet, both by food prices and lack of knowledge of proper food. In fact, people eat what they can afford and not what they need. The situation was aptly compared to Hobson's choice. Hobson's customers, you will recall, had to take the horse nearest the stable door whether they liked it or not. It was further pointed out how difficult it was to educate the masses about food requirements.

The air raid precautions proved enlightening to me. For the actual raid there were underground shelters, all of which were lined with corrugated sheet metal and were half under the ground and covered with earth and sandbags. These were bomb splinter proof but not proof against a direct hit. Each shelter was provided with two entrances in case one became blocked, and each was equipped with a spade in the event that it became necessary to dig out. Some of the shelters were furnished with a few comforts and food, but most of them were like old-fashioned, barren, storm cellars. Every householder had a shelter in his backyard, and there were many public ones located in parks and public gardens for those who might be abroad during a raid. There was a tendency for civilians to stand outside during air-raid alarms to see what was going on, and as a result, several were wounded by shrapnel from their own antiaircraft guns. No doubt with the war in its present stage, full advantage of shelter will be taken. During my visit no bombing raids occurred, but German scouting aircraft were over several times each week. Many of the public buildings were protected with sandbags, and large glass windows were either removed or boarded over. The shops, like those in Paris, had covered their show windows with adhesive tape to prevent splintering.

First aid posts were distributed throughout the city to provide immediate care for wounded civilians. From these posts the seriously wounded would be sent to the hospital for that area, and from there patients would be evacuated to safer areas as soon as possible. Each hospital has organized operating teams and has arranged to expedite the rapid handling of many casualties. Extensive preparations for blood transfusions and the administration of parenteral fluids and of gas-gangrene antitoxin have been made. Needless to say, the medical profession has worked literally day and night to prepare for the effects of total war.

A large number of firemen and air raid wardens were constantly on duty to help battle expected fires and confusion. Everyone from infancy upward was provided with a gas mask, but few people bothered to carry them until Germany invaded Holland and Belgium. Thereafter people started keeping their masks with them.

The two medical schools in Edinburgh, the Royal College of Surgeons and the University of Edinburgh Medical School, were functioning in a more or less normal fashion. The medical schools in Glasgow and Aberdeen were also carrying on, whereas those in London and Paris were evacuated at the start of the war. The students seemed to me much younger than those in America, and

there were many more women students. As yet the medical students have not been called into the army but they all have a part in the civilian air-raid precautions either in first-aid posts or in operating teams.

I worked as clinical assistant on Professor J. R. Learmonth's ward at the Royal Infirmary and found it most interesting. The infirmary is the largest voluntary hospital in the United Kingdom and has a proud history. A wealth of clinical material flowed into all its departments despite the fact that admissions were limited to urgent cases for the duration." The run of cases was much like that of any general surgical service, except that a large number were the result of coal-mine accidents and during the blackouts, of road accidents. There are seven surgical services, each of which is a complete unit and is headed by one of the senior surgeons—Professor J. R. Learmonth, Sir John Fraser, Mr. J. M. Graham, Mr. W. Quarry Wood, Mr. W. J. Stewart, Mr. A. Pine Watson and Mr. Frank E. Jardine. Each service operates twice weekly plus one day a week for receiving emergencies. Both a male and female ward of thirty-six beds are assigned to each service, and six beds on every ward are kept free for possible civilian air-raid casualties. It was quite striking to note the large number of old people in the hospital. This was due, of course, to the fact that the majority of the younger groups were in the army or in other war work. This predominance of elderly people would make evacuation of the patients difficult in the event of an air raid particularly because most of the buildings are old and have outdated physical equipment.

There were numerous empty hospitals in and about Edinburgh which were awaiting the war wounded. Some had been rapidly erected for this purpose, and others were older hospitals that had been remodeled to meet the expected needs. Hospital ships carrying wounded soldiers were expected on several occasions but docked elsewhere.

While I was there, all soldiers and sailors were treated in military hospitals. However when any of the German citizens who were interned nearby became ill, they were treated at the Royal Infirmary. One of these interned Germans was interesting. He was a young man with a lump in his neck which had been biopsied in Germany about a year before. He was brought into the infirmary for another biopsy and was placed on the police ward. His knowledge of English was so very poor that when he was given his preoperative medication he was firmly convinced that the "brutal English" were going to torture him. It took several days for him to get over his fear of English-speaking doctors.

The Edinburgh surgeons do excellent work, and their surgical judgment and anatomical knowledge seemed to me unparalleled. Their surgical technique is different from that of most American surgeons in that assistants are not used so much and they saw much more with their fingers. Continuous chromic catgut was the usual suture material except on the skin, where silk worm gut was used. It was of interest to note that they did not place any sutures in the subcutaneous fat but depended on the skin sutures and dressing to close the dead space. In a series of ninety-five clean wounds that I observed six became infected and one contained a collection of serum. Since a goodly number of surgeons, both young and old were in the army the staff was somewhat short-handed. However everyone carried the extra load in a splendid spirit. The Wilkie Surgical Research Laboratory is an excellently arranged and equipped laboratory at the University of Edinburgh but during wartime very little research work is being carried out there.

On May 6 I went to Glasgow to visit the Western In-

firmary where Professor F. C. W. Illingworth is head of the Glasgow University Department of Surgery. It was at this hospital that Joseph Lister did his first work on asepsis. The hospital has a beautiful location on a hill from which the balloon barrage along the River Clyde is easily visible. Glasgow at that time did not appear so warlike as Edinburgh but there were many French troops about, presumably en route to Norway. Four days later I went to Aberdeen to visit its medical school and the Royal Infirmary. Both these institutions are quite new and modern and, physically at least, appeared more American than those in Glasgow and Edinburgh. The countryside around Aberdeen and Glasgow is beautiful. Loch Lomond is only a few miles from the latter and the Highlands only a few miles from the former.

While I was in Aberdeen the Germans invaded Holland and Belgium and there arose considerable excitement in Britain about persons belonging to the "Fifth Column." Because of this feeling the government issued a proclamation that all aliens must report to the police daily must not leave town, must not ride in any conveyance except a public one, and must be in their living quarters from 8 p.m. until 6 a.m. To my chagrin, Americans were regarded as aliens. This regulation only applied to protected areas such as Edinburgh, Aberdeen and London. It was also rumored that the French-Italian frontier would soon be closed. Since it was obvious that travel was not going to be easy I decided on May 14 to leave for Italy while I could.

I had a reservation on the *S.S. Manhattan* sailing from Genoa on June 1 and was fortunate in having an exit permit and a permit to take money out of the country. I saw the censors May 14 and had my luggage examined and sealed. On May 15 I left for London. By then people were expecting the worst at any time. On May 16 after having had nine airplane passages to Paris canceled, I got a second plane late in the day but not until after the customs officials had confiscated my camera. This mode of travel was necessary because civilians were not allowed to cross the channel by boat. I reached Paris about 6 p.m. and boarded the 8.30 p.m. train for Genoa. The railroad station was packed with refugees and was not a pretty sight. Most of these people were dry-eyed but looked as if they had been through hell. The train also was crowded with people attempting to get to Genoa to obtain passage to America, and any sort of a seat was at a premium. The customs inspection at the French-Italian frontier was painfully thorough. When we entered Italy troops could be seen moving constantly along the roads toward the frontier. I arrived in Genoa late in the afternoon of May 17 and found the *S.S. Washington* was slated to sail the next day. Fortunately I was able to exchange my reservation on the *Manhattan* for one on the *Washington*. The few Italians that I could converse with in English were not keen on war but were ready to do what they were told.

The voyage back was without event. The contraband search at Gibraltar required only about eight hours instead of the previous forty-eight, and there were noticeably fewer merchant vessels in the harbor. The only things suggestive of war were two British submarines cruising submerged in the harbor. After the *Washington* entered the Atlantic, we did see a large convoy of allied merchantmen.

The *Washington* was very crowded. Coils had been placed in all the staterooms, and deck space for exercising or sunning was at a premium. A goodly number of the passengers were refugees from the warring nations of Europe who hoped eventually to become American citizens. Very few of them talked about their past or com-

plained about the ships being crowded, because they were so glad to be on their way to the United States. The remainder, some five hundred, were Americans returning home. Everyone was obviously happy on the thought of reaching America again. I know that I certainly was.

THOMAS W. BOTSFORD, M.D.

Peter Bent Brigham Hospital,  
Boston

## REPORT OF MEETING

### HARVARD MEDICAL SOCIETY

A regular meeting of the Harvard Medical Society was held at the Peter Bent Brigham Hospital on April 9, with Dr. Soma Weiss presiding.

The medical case presented was that of a nineteen-year-old girl, who entered the hospital because of dyspnea, weakness and pallor. At twelve years of age she experienced six weeks of migratory polyarthritides. The following year menstruation began, the periods were irregular and profuse and lasted from nine to thirteen days. In November, 1938, the patient first noted exertional dyspnea and afternoon ankle edema but continued going to school until the following May when she was obliged to retire to bed due to excess fatigue. In August, 1939, she felt better but still required eighteen hours a day in bed and had episodes of fainting. A local physician was consulted in March, 1940, and he prescribed liver extract and iron. Physical examination on admission revealed a pale young woman in whom merely sitting up in bed occasioned extreme dyspnea. The pulse was 150, and the respirations 40. The heart was enlarged to the left, and there was an apical systolic thrill and a loud and metallic aortic second sound, associated with an aortic systolic murmur. The uterus was retroverted, retrogressed and nodular, and there was rather profuse vaginal bleeding. The hemoglobin was 15 per cent, the red-cell count 1,200,000, and the hematocrit 10 per cent. Treatment consisted of 2000 cc. of whole blood in repeated transfusions, with a rise of the hemoglobin to 61 per cent, of the red blood cells to 3,450,000 and of the hematocrit to 31 per cent in eight days.

In discussing the case, Dr. John G. Gibson, 2nd, emphasized the importance of large amounts of blood in combating serious degrees of anemia. Dr. Elliott C. Cutler questioned the wisdom of transfusions in patients who have one large hemorrhage and are not expected to have another. He reasoned that such a procedure may remove the stimulus for regeneration in the bone marrow. Dr. Soma Weiss stated that the patient probably had no heart trouble other than anemia, but he warned that occasionally such a myocardium may fail to respond completely and that this may result in residual myocardial disease.

The surgical case was that of a sixty-nine-year-old man admitted on January 29, 1940, after allegedly being struck by an automobile half an hour prior to entry. There had been no period of unconsciousness before admission, and his memory for details was good. Physical examination revealed a 15-cm. laceration of the scalp and a compound comminuted fracture of the right lower leg. The patient was in incipient shock with a pulse of 100 which was moderately weak. The blood pressure was 90 systolic, 50 diastolic. The patient appeared gray and anxious. Dry sterile dressings were applied to the wounds, and the patient was put in a moderate Trendelenburg position and covered with blankets. Fifteen milligrams of morphine

sulfate was administered after a neurological examination was found to be negative. Roentgenograms were immediately taken of the leg but none of the skull, and the patient was taken to the operating room for a transfusion. There were signs of improvement after 500 cc. of blood, followed by 1000 cc. of normal saline, had been given, debridement of the leg wound was carried out, and plaster was applied over a dry sterile dressing. Simultaneously there were carried out debridement, cleansing and tight suture of the scalp wound. After the danger of shock had passed, subsequent manipulation of the leg was performed. Laboratory data on entry showed a hemoglobin of 90 per cent, a red-cell count of 4,500,000, a white cell count of 20,000 and a hematocrit of 46 per cent. On the second day the hemoglobin fell to 60 per cent, the red-cell count to 3,400,000 and the hematocrit to 36 per cent. Another blood transfusion and the administration of ferrous sulfate brought about a gradual return to normal values. Dr. Cutler alluded to the fact that a systolic blood pressure of 90 is really serious in a patient whose original level was 170 to 190.

The first speaker of the evening was Dr. Gibson, who discussed "Experimental Observations on the Physiology of Shock," based on experiments on burns. It was pointed out that the fault is essentially a peripheral rather than a central one. The important changes observed were diminished blood volume, which amounted to about one fifth of the total volume, increased viscosity of the blood and a rapid pulse. The respirations, mean arterial blood pressure and oxygen saturation remained about the same until terminally when the blood pressure showed a sharp drop and oxygen saturation fell to low levels. The mechanism is considered to be a loss of fluid into the site of injury, with subsequent compensatory sympathico-adrenal activity which may finally augment the effect of the noxious agent. An increase in capillary permeability resulting from anoxia may also play a role in the continued loss of fluid. The effects of various types of treatment proved that nothing helped late and that plasma was the best remedy early. Fifty per cent glucose was of only temporary benefit, while normal saline caused transitory dilution of the circulating blood. Whole blood seemed to cause an increase in viscosity with no marked improvement in the circulating blood volume.

Dr. J. Englebert Dunphy continued with "Observations on the Pathology of Shock." By studying the changes during various phases of shock it was determined that in the early stages of traumatic shock significant pathologic changes are confined to the site of injury. In the late stages of shock there are generalized pathologic changes, characterized by capillary dilatation, congestion and edema throughout the lungs, liver, kidney and gastrointestinal tract. New changes, however, were not so marked as those described by Moon. There were changes in the adrenal gland which consisted of polymorphonuclear leucocytic infiltration and capillary congestion of the zona fasciculata. These occurred early in the shock period and were not simply a manifestation of generalized normal congestion. Whether the late changes were toxic or ischemic and hence due to lack of oxygen was not determined. It was found that the use of infusions of plasma were the most effective means of maintaining the blood volume at normal levels. However, although the late pathologic changes of shock were minimized by maintaining the blood volume at normal levels, these were not entirely prevented. This suggests that some factor other than blood volume is involved in the pathogenesis of shock.

The "Clinical Aspects of Shock" were discussed by Dr. Eugene A. Stead, Jr. After recounting the great groups

of cases in which shock may be observed the speaker reminded the audience of the difficulty in interpreting animal experiments because so many factors influence the time of onset of shock. Dr. Stead differentiated the clinical signs of shock with and without arteriolar constriction. He stated that the latter type responds better to transfusion, while the peripheral blood pressure in the former cannot be used as a criterion for treatment and prognosis. Observations on blood loss indicate that no signs are present until more than 500 cc. are lost and that when the frank manifestations of shock appear treatment may already be of no avail. An important prognostic finding is the plasma-protein value for patients with a poor reserve fail to regain and maintain an adequate circulation volume and do poorly on the whole.

## NOTICES

### ANNOUNCEMENT

ALFRED HURWITZ, M.D., announces the removal of his office from 483 Beacon Street to 113 Bay State Road, Boston.

### AMERICAN BOARD OF OPHTHALMOLOGY

There will be only one written examination during 1941. This will be held in various cities throughout the country on March 8. Candidates enrolled in the Preparatory Group who have been advised that they will be eligible for examination during 1941 should make application at once to take this written examination.

Application must be made on the regular blanks provided for the purpose and must be received before December 1, 1940.

Oral examinations in 1941 will be held at Cleveland in May or June and at a place to be announced in October the deadlines for submitting case reports are February 1 and July 1 respectively. A special oral and clinical examination will be held on the Pacific Coast during 1941 provided there are enough candidates to warrant it. Applications for this examination should be filed before September 1, 1940 so that the Board may complete necessary arrangements.

All candidates planning to take the examination in 1941 should write at once to the Board Office for formal application blanks, indicating their preference of examination place. Letters should be addressed to American Board of Ophthalmology 6830 Waterman Avenue, St. Louis, Missouri.

### SOCIETY MEETINGS AND CONFERENCES

- SEPTEMBER 2-6—American Congress of Physical Therapy Page 362 issue of May 16.
- OCTOBER 6-11—Annual meeting of the American Academy of Ophthalmology and Otolaryngology Page 31 issue of July 11.
- OCTOBER 8-11—American Public Health Association Page 655 issue of April 11.
- OCTOBER 11-12—Pan American Congress of Ophthalmology Page 378, issue of May 13.
- OCTOBER 14-25—1940 Graduate Portfolio of the New York Academy of Medicine. Page 938, issue of May 30.
- OCTOBER 21—American Board of Internal Medicine. Page 399 issue of February 29.
- JANUARY 4, 1941—American Board of Obstetrics and Gynecology Page 194 issue of January 20.
- APRIL 21-25, 1941—American College of Physicians. Page 1065 issue of June 20.
- MARCH 8, 1941—American Board of Ophthalmology Notice here.

## BOOK REVIEWS

*The Kosher Code of the Orthodox Jew: Being a literal translation of that portion of the sixteenth-century codification of the Babylonian Talmud which describes such deficiencies as render animals unfit for food (Hilkot Teretot Shulhan Arukh) to which is appended a discussion of Talmudic anatomy in the light of the science of its day and of the present time.* By S. I. Levin and Edward A. Boyden Ph.D. 8 cloth 243 pp., with 5 illustrations. Minneapolis: University of Minnesota Press, 1940. \$4.50.

From the dawn of Jewish history medicine exercised a special interest on the Jewish mind. Medicine was an integral part of the ritual life. The vast subject of "uncleanliness in connection with defilement from dead bodies, menstruation and its disorders, leprosy and so forth had its actual medical bearing. It is for these reasons that the medical historian, Dr. J. H. Boas, states "It corresponds in the reality in both the actual and chronological point of view to consider the Jewish as the creators of the science of public hygiene." Furthermore, the Biblical prohibition of eating any flesh that is "born of the beasts of the field" (Teretot) or anything that "die of itself" gave rise to dietary regulations which included the postmortem examination of animals destined for food. These investigations resulted in the accumulation of a very practical knowledge of animal anatomy and physiology by the rabbis who specialized in this field of research. Although these facts are scattered throughout their religious literature a systematic body of anatomical and medical knowledge did not develop. It is from this point of view that the authors of this book make a distinct contribution. Rabbi Levin and Professor Boyden have given us, for the first time, a literal translation in English of that portion of the sixteenth-century codification of the Babylonian Talmud which describes such deficiencies as render animals unfit for food (Hilkot Teretot, Shulhan Arukh). The translation is accurate and literal and for this reason it reflects the terseness of the text. It preserves the original flavor of this vernacular account, and also provides an accurate source material. Of great value to the student of medical history are the numerous notes appended to the text. With the patience of a true scientist, Professor Boyden has discussed each term of Talmudic anatomy in the light both of the science of its day and of that of the present time. This volume should be a valuable addition to the library of all students of medical history.

*Illustrations of Bandaging and First Aid.* Compiled by Louis Oakes, S.R.N., D.N. (Leeds and London) 8 cloth, 248 pp., with 108 plates. Baltimore: Williams & Wilkins Company 1940. \$2.00.

The aim of the book, according to the author is "to enable the student, by means of pictures to quickly master the science and art of bandaging and of first-aid in fractures and hemorrhages."

The illustrations consist of 290 photographs, many of which have been touched up to emphasize the edges of bandages and the directions in which folds and knots take place. On the whole the illustrations serve very well to clarify the brief outlined text. Nearly half the book is given over to elaborate description of the many fold methods of using a triangular bandage. The remainder concerns itself with roller bandaging and first aid in hemorrhages and fractures. The latter sections



take no recognition of many of the changes in practice that have taken place during the last few decades, for example, the section dealing with fractures at no point mentions traction splints or the use of traction. Many of the text instructions are so brief as to be of no particular value to the student, thus the instruction for control of hemorrhage from the dorsalis pedis artery simply states "Place the thumb over the lower end of the tibia."

The author, a teacher in nursing, has apparently written the book for the use of lay groups whose war work may involve them in the need for rendering first aid. It is distinctly less useful than many of the manuals of first aid that are already available in this country.

*King Gustaf V's Stockholm Jubilee Clinic for Radiotherapy and Research in Cancer. A description.* By Gosta Forssell, Elis Berven, Olle Reuterwall and Rolf Sievert. 8°, paper, 80 pp., with 8 plans and 32 illustrations. Stockholm P. A. Norstedt & Soner, 1939. Swed. kr. 8.

Sweden has long been in the forefront of advance in roentgen and radium treatment. At the Roentgen Institute of the Serafimer Hospital and at the Caroline Hospital, both in Stockholm, many advances have been reported in the last thirty years. A new clinic has recently been opened. This book describes in detail not only the work done at the clinic, but also the new building. There are many illustrations as well as plans of this superb center for research and treatment.

*Short Stature and Height Increase.* By C. J. Gerling. 8°, cloth, 159 pp., with 5 illustrations. New York: Harvest House, 1939. \$3.00.

The author has attempted to write a book on the subject of stature, weight and height for the lay public. He has tried to correlate endocrinology, food and nutrition, inherited characteristics and an individual's occupation with respect to his appearance. However, the entire subject is considered in a sketchy manner, with errors of omission rather than commission. The facts are presented in a loose way, and the use of scientific terms to add authority is deplorable. The failure to explain clearly or to qualify statements makes the entire text a potpourri which cannot be recommended to even the layman.

*Sexual Disorders in the Male.* By Kenneth Walker, F.R.C.S., and Eric B. Strauss, D.M. F.R.C.P., with a foreword by Sir Walter Langdon Brown, M.A., M.D., D.Sc., F.R.C.P. 8°, cloth, 248 pp., with 9 illustrations. Baltimore: Williams & Wilkins Company, 1939. \$3.00.

This treatise is unique in that it combines, in happy proportion, the point of view of the urologist and that of the psychiatrist. The book is well arranged, in the first portion are included the known facts relating to the physical aspects of the sexual organs in so far as they have to do with the sex function, while the second part gives the psychopathology of sexual deviations and the measures that may be taken to remedy these defects.

In presenting the facts underlying the behavior of the sexual function, the authors have taken nothing for granted and have avoided a repetition of statements, the truth of which is based solely upon frequent reiteration. The entire situation has been appraised in the light of recent neurological and hormonal studies. The section dealing with the psychiatric aspect of the problem states clearly and simply the problems involved and outlines their treatment.

The book as a whole is characterized by the moderation,

balance and sanity of the writers' opinions, and by a method of presentation of intimate details which avoids completely any offense to the sensibilities of the reader. It is by far the best book on this subject which the reviewer has seen.

*Displacement of the Calcified Pineal Body in Roentgen Pictures as an Aid in Diagnosing Intracranial Tumours. An anthropometrical statistical analysis.* By Bengt Lilja. 8°, paper, 182 pp., 40 tables. Stockholm: P. A. Norstedt & Soner, 1939. Swed. kr. 10.

It has long been recognized that displacement of the pineal body is an important sign in indicating intracranial tumors. Fortunately, the pineal gland is calcified in a large percentage of cases. The author of this monograph has carefully verified the position of the gland in a large group of normal individuals, he found that it is visible by x-ray in at least 40 per cent of the subjects examined. He then examined 80 cases of proved intracranial tumor and noted that 37 per cent showed a displacement of the pineal body. He gives exact measurements for such displacements, showing the variations in the position of the body which can be considered normal. This research, on a highly technical subject, can be strongly recommended to those who are interested.

*Frontier Doctor.* By Uring C. Coe, M.D. 8°, cloth, 264 pp. New York: MacMillan Company, 1939. \$2.50.

This is a well written and interesting story of a young medical graduate, who in 1905 went far up into central Oregon, over one hundred miles from the nearest railroad station. There in a small lumbering town he practiced for thirty years. His experiences are of great interest, as this was the last frontier to be opened in America, and he might be well termed the last of the frontier doctors. The book is full of exciting stories of his adventures with the roughest type of individuals. It should be noted that he, as a physician, held a high place in the community and was immune from assault. His endeavors were usually appreciated, and many a life was saved by his activities. He eventually became the leading citizen of Farewell Bend, Oregon. This book can be highly recommended as a straightforward and honest account of a fine physician who upheld all the best traditions of the profession.

*The Surgery of Injury and Plastic Repair.* By Samuel Fomon, Ph.D., M.D. 4°, cloth, 1409 pp., with 925 illustrations. Baltimore: Williams & Wilkins Company, 1939. \$15.00.

This large compilation, consisting of twenty chapters, represents great industry. The first nine chapters are devoted to general principles, such as tissue transplantation, wounds, fluid, salt and acid-base balance and so forth. The remaining chapters concern regional surgery of the exterior head,—cranium, nose, eyelid, auricle, lip and so forth. In the preface the author states that it was his "original aim to treat of the entire body." It is his intention "to add in the near future another volume." The author apparently plans to have the rather disproportionate section in the present volume devoted to general principles serve also for the coming volume. Each chapter is followed by a list of references, alphabetically arranged and totaling 2700 authors, of which about two thirds are referred to in the text. There are numerous cuts, many of which consist of several illustrations. These are well selected and form valuable additions to the text. There is a good double-column index of 18 pages.

The large volume is durably bound. The paper and typography are excellent.

*Hygiène et cancer* By P. Delore. 16 paper 52 pp. Paris Presses Universitaires de France, 1939. 6 Fr. fr.

This poorly printed little handbook is of but little interest or value.

*Gynecologic Operations and Their Topographic Anatomic Fundamentals* By Heinrich Martus, M.D. Translated by W. A. Newman Dorland. 4 cloth 486 pp. with 404 illustrations, mostly colored. Chicago S. B. Debour 1939. \$10.00

This volume, written by the director of the University Women's Clinic in Göttingen, is devoted entirely to gynecologic surgical technique. Standard gynecologic procedures are described as well as the more unusual and difficult operations such as the radical hysterectomy of Wertheim. The description and illustration of operative procedures for urinary fistulas are of particular merit. There are differences in detail between the procedures described by Martus and those commonly used in this country but on the whole they are quite similar.

Since diagnostic procedures and indications for operation are not discussed but only mentioned briefly the book must be used as a supplement to other gynecologic works. The greatest usefulness of this book will be in the surgeon's room of the hospital where the staff can consult it readily about operative questions.

The illustrations are plentiful and clear so that each operation can be readily understood. The workmanship in the book is of the best.

*Berzelius-Porträtt*. Arne Holmberg. 4 paper 32 pp. with 35 illustrations and 32 full-sized plates. Stockholm Almqvist & Wiksell, 1939

This is a brief account of Berzelius, with a short bibliography. It is accompanied by thirty-two superb plates showing statues, medals, drawings and paintings of the great Swedish scientist at various stages of his life. The book is a splendid addition to facts concerning this great man, whose anniversary has recently been commemorated by a Swedish postage stamp in his honor.

*The Patient as a Person. A study of the social aspects of illness.* G. Canby Robinson M.D., LL.D., Sc.D. 8<sup>1</sup> cloth 423 pp. New York The Commonwealth Fund 1939. \$3.00.

A quickening of interest in the social aspects of disease has become evident in many places. The outlook of a man in whom this interest has been active for more than thirty years has been used here to guide the assembling and presentation of social data on a series of ordinary urban hospital cases. The result is essentially a book of social case histories, somewhat stereotyped but nevertheless recording a large amount of diligent labor.

Frequently interspersed comments provide a prolonged argument for greater emphasis on the subjective elements of the practice of medicine. The reviewer could not escape the feeling that he and his fellow practitioners were being gently reprimanded. There is in the book some thing of the social workers' conviction that one can always find what one looks for and there are repeated asseverations that "adverse social conditions produce excessive emotional reactions." No attempt is made to suggest the reversibility of this dictum.

For hospital-bound professors of medicine, for medical students and for some specialists and consultants the book has much value. Those who have successfully practiced medicine will judge it commonplace.

*Poliomyelitis in the City of Melbourne 1937-8* By Hilda W. Bull B.Sc. M.B. B.S., D.P.H. 4 paper 56 pp., with maps, charts and tables. Melbourne: Health Committee of the Melbourne City Council, 1939. Complimentary.

The medical officer of the Department of Health Melbourne (Australia) City Council has published an extensive account of an epidemic of poliomyelitis that devastated the city a few years ago. This is accompanied by maps showing the beginning of the epidemic, the meteorological data and the spread of the epidemic through the various sections of the city and a somewhat detailed account of the 174 cases and the 199 abortive infections which occurred in a population of about 92,000. Seven per cent of the paralytic cases died and only 6 of the definite cases recovered without paralysis. It is believed that the installation of a number of respirators saved many lives. The epidemic, in general did not differ from those which have preceded it, but another important account has been made of an outstanding epidemic disease. The care with which this record has been compiled deserves particular commendation.

*Précis de médecine des enfants* P. Nobécourt. Sixth edition, entirely revised. 8 cloth 1303 pp. with 604 illustrations. Paris Masson et Cie, 1939. 175 Fr. fr.

When a scientific textbook passes through as many editions as has this book, it may be taken for granted that it has served, and is still serving a very useful purpose. But its value to Dr. Nobécourt's compatriots is one thing; its value to the average American reader another. The latter will not perhaps resort to a treatise in a foreign tongue, except for two very special reasons—either because it embodies an original piece of research, or because its point of view or method of approach differs from the ordinary. There is nothing novel here in either direction. This is not used to belittle the book, but simply to point out that it contains no more matter nor matter much differently presented than is available in texts printed in English which at least for most of us are easier to use.

The book is safe and sane, one which though concise is comprehensive in scope, covering indeed the whole field of pediatrics with the exception of infant feeding. It is well printed, well illustrated and more convenient to handle than the majority of medical texts. One grave fault is the lack of an index. Such an omission is always exasperating and often enough leads to indifference to a book which really ought not to be neglected.

*Endocrine Gynecology* By E. C. Hamblen, B.S., M.D., F.A.C.S., with a foreword by J. B. Collip M.D. 4 cloth 453 pp., with 169 illustrations. Springfield, Illinois Charles C. Thomas 1939. \$5.50.

This book is very useful and worth while. It should be valuable to those with but little understanding of female endocrinology. It should increase the knowledge of those with a fair understanding and it should be important as a reference book to those participating in endocrine investigations. The plan of the book is sound; descriptions of normal physiology are clear and personal deductions are helpful. There are a few omissions, among them Albright's disease, panhypopituitarism following obstetric

calmities, senile osteoporosis and "17 ketosteroid" determinations. The author's observations of the effect of progesterone on abnormal bleeding will not be accepted everywhere. Where there is incomplete agreement of any point the author is careful to present evidence on both sides, including his own, and he does not make dogmatic statements.

This book should be read by practitioners, surgeons and gynecologists, and from it a much better understanding of functional changes will be had. The book is highly recommended.

*Miss Susie Slagle's* By Augusta Tucker 8°, cloth, 332 pp. New York and London Harper & Brothers, 1939 \$2.50

This is a novel with considerable medical interest. The scene is laid in Baltimore, during the early days of the Johns Hopkins Hospital and University School of Medicine. Miss Slagle runs a medical boarding house, and the principal characters are young medical students. Incidentally, there is mention of the famous teachers of medicine, such as Kelly, Halsted, Welch and Osler. Unfortunately the story is not very interesting, nor is it an excellent picture of medical school life. The author has missed a fine opportunity to depict the young doctor in the making. One can read the book with a fair amount of interest, but the story fails to hold the attention of the reader. Except for a few scattered pages, one cannot recommend this book as a medical item.

*The Inter-Relationship of Mind and Body. The proceedings of the association, New York, December 27th and 28th, 1938.* Association for Research in Nervous and Mental Disease. Vol. XIX of a series of research publications. Editorial Board: Foster Kennedy, Angus M. Frantz, and Clarence C. Hare. 8°, cloth, 381 pp., with 28 illustrations and 10 tables. \$6.00

This book is a summary of the papers read before the Association for Research in Nervous and Mental Diseases, at the meeting held in New York City in December, 1938. During the meeting particular attention was directed toward an evaluation of the hereditary factors in mental diseases, the significance of alterations of mental and emotional processes produced by diseases of the brain, the effect of vitamin deficiency on mental and emotional processes, and topics of a similar nature. Each subject was discussed by an individual of experienced qualifications. The book has a high mean value, for none of the contributions can be considered as poor, and many of them are excellent. Its appeal will naturally be limited, but for those whose interests lie in the field of psychiatry and its many problems, this book is a welcome addition to the literature.

*Illustrations of Surgical Treatments, Instruments and Appliances* By Eric L. Farquharson, M.D., F.R.C.S.E., with a foreword by Sir John Fraser. 8°, cloth, 338 pp., with 259 illustrations and 57 plates. Baltimore: Williams & Wilkins Company, 1939. \$6.50

While there is quite general agreement throughout the world with regard to the basic principles of surgical treatment, in the actual mechanical application of these principles every surgeon becomes a rugged individualist. No two surgeons, for example, would apply a plaster boot for an ankle fracture in exactly the same way. In this book, the author presents the art and craft of surgery as practiced at the Royal Infirmary, Edinburgh, in relation to intravenous infusions, transfusions, the common fractures and minor orthopedic conditions. Many of the procedures described are credited to Boehler, but are better presented and illustrated than in his textbook. In this

country, the advocated treatment of fractures of the pelvic girdle will not receive much support, nor can the immediate strapping of sprains be recommended. Although the use of various types of adhesive tape is well described, there is no mention of any method of protection of the skin beneath the tape, such as painting with compound tincture of benzoin. The last two thirds of the book is devoted to illustrations and descriptions of the instruments and appliances commonly used on the general surgical service.

The book should be of particular interest to the junior student of surgery and to the surgeon called on to treat fractures.

*Vitamin D. Chemistry, physiology, pharmacology, pathology, experimental and clinical investigations* By C. I. Reed, Ph.D., H. C. Struck, Ph.D., and I. E. Steck, M.D. 8°, cloth, 371 pp. Chicago: University of Chicago Press, 1939. \$4.50

This remarkable world has for the past decade enjoyed a promotion of vitamins for the treatment of all and sundry conditions. Since vitamins are directly related to health, just as are water balance, sleep and proper food, the public has been taught to accept vitamin preparations as specific antidotes and to expect their physicians to uphold this view. Hand in hand with this situation there has appeared an enormous scientific literature on the subject of vitamins.

To help us all, monographs reviewing the subject are written, it is with this intent that the authors have presented the volume on vitamin D, its chemistry, physiology and medical uses. On the whole the text is good, but the reader should be cautioned against the claims made for this vitamin in the treatment of arthritis. With this exception, the book is to be recommended without restriction, for the summaries are carefully written. To the entire text is added an extensive bibliography. The book should serve all those working on problems of nutrition, interested physicians, and, in particular, the pediatrician who today must properly evaluate the use of vitamins.

*A Doctor Without a Country* By Thomas A. Lambie, M.D., Sc.D., F.R.G.S., with an introduction by Howard A. Kelly, M.D., F.A.C.S., LL.D. 8°, cloth, 252 pp., with 6 illustrations. New York: Fleming H. Revell Co., 1939. \$2.00

Dr. Lambie, who comes from an old Maryland family, devoted his early medical life as a missionary, far up the River Nile in a small United Presbyterian mission in which he was the only doctor. His life is described in considerable detail. There is a strong religious element in the man, which is apparent at all times. Although he seems to have been a sound surgeon and good physician, his life was closely woven with this strong religious bent. Later, he went to Ethiopia where he built a hospital just before the evacuation of the country and the overcoming of the Ethiopians by the Italians. He was on intimate terms with all the notable people in Ethiopia, and the last third of the book is by far the most interesting part, giving as it does a detailed story of the final days of Ethiopia as a nation. The book suffers from a somewhat stilted style, and it cannot be read with avid interest. It is a little too factual to make the narrative run smoothly. Nevertheless, many medical men should be enlightened by the book, which appears to be a straightforward, honest account of a doctor's unusual travels. The make up and the title of the book leave much to be desired, the illustrations are not of any great value. It is recommended, however, for those who are interested in the subject, and particularly all young physicians embarking on the arduous life of a missionary doctor.

# The New England Journal of Medicine

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VOLUME 223

AUGUST 8, 1940

NUMBER 6

## THE SURGICAL TREATMENT OF CARCINOMA OF THE PROSTATE\*

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BALTIMORE

IN ANY study of disease, it is interesting to read the early literature and to contrast with it our present views and methods. Our present knowledge of carcinoma of the prostate has developed to such an extent that everyone recognizes the relative frequency of its occurrence, so that it is somewhat of a surprise to read that Wolff,<sup>1</sup> only as long ago as 1899, could find but 83 cases reported in the literature up to that date. In 1906, Young<sup>2</sup> first called attention to the frequency of carcinoma of the prostate, in an analysis of 318 cases of prostatic obstruction in which he found 68 cases of cancer (21 per cent). Four recent articles have appeared which demonstrate, without any question, the great frequency of this condition. Muir<sup>3</sup> in 1934, in routine autopsies on men over sixty found an incidence of 13 per cent in whom carcinomatous areas were seen on sections from the prostate gland. Rich,<sup>4</sup> in 1935, in 292 consecutive autopsies on men over fifty dying on all services of the Johns Hopkins Hospital, found an incidence of 14 per cent. He concluded that the true incidence must be very much higher, because he studied only one routine section of the prostate gland in each case, and therefore must have missed some areas of malignancy in at least some of the cases. Moore,<sup>5</sup> in a series of routine autopsies at Viennese hospitals in which serial sections were cut, found an incidence of 17 per cent. Gaynor,<sup>6</sup> in 1938, in an extensive report on the pathology of prostatic carcinoma, studied multiple sections of the gland in 1000 autopsies on men over forty and found an incidence of 18.4 per cent. Thus, in a relatively short space of time, the conception of this disease has been changed from that of a clinical rarity to that of one of the most frequent malignant diseases affecting men.

Gaynor confirmed the observation of Moore

and of Rich that the incidence increased with age, 38.7 per cent of his cases in which the patients were eighty to eighty nine years of age were found to show malignant disease. He also made the interesting observation that in some of his cases two or even three distinct primary growths could be demonstrated. These studies of such early carcinomas are particularly interesting as they present conclusive evidence as to the origin of the growth, which is, of course, of great clinical significance.

In a study of operative specimens in which both carcinoma and benign prostatic hypertrophy were present, Geraghty,<sup>7</sup> in 1922, found that with a single exception the posterior lobe was carcinomatous. In Moore's autopsy series, the carcinoma was localized in the posterior lobe in 73.5 per cent of cases. Rich notes that the growths are situated near the outer margins of the gland and that there is a tendency to invade the capsule and states that carcinoma may arise also within the newly formed tissue of a nodular hypertrophy but that the situation of the early tumor suggests that the non-hypertrophied prostatic senile tissue and compressed atrophic glands are the favorite sites of origin. Gaynor found the posterior lobe involved in 60 per cent of cases, the anterior lobe in 29 per cent, the lateral lobes in only 10 per cent and the middle lobe in 0.5 per cent. He found moreover, that in 98.5 per cent of his cases the neoplasm began at the periphery of the lobes.

In early carcinoma of the prostate, a small nodule first appears which extends slowly upward in the region of the seminal vesicles, later infiltrating the whole gland and the region beneath the trigone, but usually only in the terminal stages does it invade the muscular wall or mucosa of the bladder. Microscopic infiltration of the pericapsular lymphatics can be demonstrated followed by metastases to the pelvic glands and thence characteristically, to the bones of the pelvis. Depending

From the Brady Urological Institute, Johns Hopkins Hospital, Baltimore.  
Read before the New England Branch of the American Urological Association, November 9, 1939.

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on the degree of infiltration around the neck of the bladder, there is a varying degree of urinary obstruction. In spite of its usual origin, less than 1 cm from the rectal wall, the latter structure is rarely invaded, because between it and the prostate there lie the surgically important anterior and posterior fascias of Denonvilliers, which are described as devoid of lymphatics and which, therefore, prevent the extension of the growth.

Clinically, carcinoma of the prostate is known as a disease of slow development. The very fact that it is symptomatically silent for a long time makes its early diagnosis extremely difficult. On account of the fact that clinical symptoms usually do not occur until the growth has progressed to a sufficient degree to cause urinary obstruction, metastases are often present when the patient is first seen. In Bumpus's<sup>8</sup> series, 25 per cent of patients showed metastases at their first examination, and Barney and Gilbert<sup>9</sup> noted metastases in 58 per cent.

From this brief consideration of the main facts that we know about the origin, extension and metastases of this disease, it is evident that an early diagnosis, before the neoplastic process has extended beyond the capsule and into the seminal vesicles, is essential chiefly on account of the fact that these patients have no symptoms of sufficient degree to require them to seek medical advice.

It is, unfortunately, a general impression among the medical profession that carcinoma of the prostate is always a hopeless disease, but there are among the records of the Brady Urological Institute reports of 91 cases in which the diagnosis was made sufficiently early to carry out a radical extirpation, all but 1 of these have been followed long enough to demonstrate beyond doubt that, if a diagnosis can be made before the disease has advanced too far, a surprisingly high proportion can be considered as surgical cures.

The diagnosis depends on the demonstration of a hard nodule or area, described either as of third-degree induration or of almost stony hardness, in the gland on rectal examination. In extensive cases there is no difficulty in making a diagnosis. In early cases, where only a small area of induration can be felt, the diagnosis may be extremely difficult, furthermore, cases of this type, unless associated with some degree of benign prostatic hypertrophy, rarely present symptoms, so that our greatest hope of recognizing them early lies in the routine medical check-up, which in all men above the age of forty-five should never be undertaken without a careful rectal examination.

Carcinoma of the prostate, from the clinical

standpoint, can be conveniently divided into four main groups.

Group 1 includes those cases which have few if any symptoms referable to the urinary tract, but in which either the growth, on rectal examination, is found to extend beyond the capsule into the membranous urethra, into the seminal vesicles or into the base of the bladder, or glands can be palpated in the perivesicular tissues. In other words, these are cases in which complete operative removal of all the malignant tissue is obviously impossible. In view of the absence of symptoms and clinical evidence of obstruction, no operative procedure should be carried out in these cases, but there is considerable divergence of opinion as to the type of treatment that should be instituted. Some clinicians believe that these patients are best left without any treatment whatsoever, and it is quite true that in some cases of this type, even though the disease is extensive when the patient is first seen, its progression, even in the presence of demonstrable metastases, may be extremely slow, so that the patient may have several years of comfort before symptoms develop. Other clinicians advise deep x-ray therapy, directed not only to the gland itself but also to the probable areas of metastasis, while still others advise radium applications given through rectal and urethral applicators or by direct implantation of radium seeds or needles into the gland itself. It is extremely difficult, even in a long series of cases, to determine accurately the true efficacy of these various methods, especially if one considers the different inherent biological qualities of each growth and the probability that microscopically and clinically similar tumors may respond differently to various forms of therapy.

It is the impression of the staff of the Brady Urological Institute that, in the majority of cases, the local growth can be made to retrogress or at least be held in control by the judicious use of a combination of radium and deep x-ray therapy. While no definite retrogression of metastatic areas has been demonstrated in the x-ray films, there is no question that pain, especially that from pressure on nerve roots, can in most cases be satisfactorily controlled, at least temporarily, by deep x-ray therapy. Therefore, in this particular group where urinary symptoms are absent, it has been our custom to institute radium and x-ray therapy. Certainly in numerous cases rectal examination has shown a most marked retrogression of the local growth, with disappearance of the characteristic nodules and areas of stony hardness, some individuals were carried through their disease until death occurred from

general metastases and cachexia, hence we believe that obstructive phenomena can often be prevented in these cases by a combination of radium and deep x ray therapy.

Group 2 includes those cases with varying degrees of obstructive symptoms and signs in which the growth has extended too far for any hope of complete operative eradication. In many clinics, this type of case is treated by some method of transurethral resection, and following the advent of this most valuable addition to the urological armamentarium, it was our custom for some years to use it almost exclusively. However in many of the larger neoplasms, especially those associated with benign prostatic hypertrophy in which considerable amounts of tissue had to be resected to relieve the obstruction, the postoperative course was complicated by persistent ulceration infection and in some cases, recurrent hematuria with resulting symptoms of pain, frequency and urgency. In this type of case, better results have been obtained by enucleation of the obstructing lobes and nodules through a perineal exposure. The postoperative result is better by this technic and the progression of the disease is definitely inhibited.

In the smaller growths which are still too far advanced for radical cure, and which resemble benign median-bar obstruction or contracture of the vesical orifice of the so-called collar type of benign hypertrophy there is no question that transurethral resection is the ideal method to employ so that, in point of fact, our attitude in regard to malignant disease is quite similar to our method of procedure in dealing with the benign obstructions in which we limit transurethral methods to the contractures the median bars, the slight degrees of intravesical collar type hypertrophies and small intraurethral intrusions.

Cases of this group were formerly treated by permanent suprapubic cystostomy and of course in those in which uremic manifestations were present there was usually a marked improvement in general health. It can scarcely be denied however that a permanent suprapubic tube is a great burden and to those condemned to such an existence, with the possibility of recurrent infection and stone formation, a life of invalidism is about all that can be expected. Therefore, the aim of any surgical procedure for these unfortunate patients should be to preserve urinary function in as nearly a normal condition as is possible under the existing circumstances.

Group 3 includes those cases without urinary symptoms in which the neoplastic growth has not extended beyond the capsule, into the membranous

urethra or beyond the bases of the seminal vesicles, but in which metastases can be demonstrated by the x-ray film. In other words were it not for the presence of these latter manifestations, one might hope by radical operation to remove completely all the tumor tissue. It seems fairly obvious that in these cases, which have neither symptoms nor signs of obstruction but in which the presence of metastases precludes the possibility of complete eradication, no operative procedure should be done, and it has been our custom to treat these cases similarly to those in Group 1 that is, by a combination of radium and deep x ray therapy. It might be argued that even in the presence of metastases complete removal of the local disease might prevent the development of future obstruction but we have found that with definite bone metastases, in many cases at least, death ensues before obstruction develops, and that conservatism is the method of choice, because by radium and x ray therapy the development of obstruction may be prevented indeed, if obstruction should ultimately develop it can be handled by transurethral resection or perineal prostatectomy, as the circumstances indicate.

Group 4 includes those cases considered suitable for Young's radical operation. The neoplastic process must not extend outside the capsule of the prostate or into the membranous urethra to any great extent or beyond the bases of the seminal vesicles. These criteria are, of course, determined by careful rectal examination. In addition there must be no metastases demonstrable on general physical examination or by x ray film. Other important factors such as the general condition of the patient his age and probable life expectancy must be carefully weighed and will eliminate some cases which might otherwise be considered as suitable for complete eradication by radical operation. It is obvious that an early diagnosis must be made if we are to recognize such cases before the disease has extended too far. Many of these patients have few obstructive symptoms, and the early lesion has been recognized in the course of the complete physical examination by a keen clinician who has found an area of suspicious induration in the prostate on rectal examination. In other individuals, more fortunate, perhaps, the early carcinoma is associated with benign prostatic hypertrophy so that the symptoms arising from the latter condition have caused him to seek competent medical advice. In any event, on account of these factors, especially the difficulty of early diagnosis, few urologists will encounter a large series of cases suitable for the radical operation until clinicians—medical surgical and urological

—have become more alert in looking for cancer of the prostate and more suspicious of even small areas of marked induration. Many more cases will then be recognized in the early stages, when hope for a radical cure by operation can still be entertained.

The diagnosis is, of course, often difficult, and the differentiation of localized sclerotic and inflammatory areas in the gland may be impossible. In a few cases, areas of tuberculous calcification or stone may be confusing, although in the latter condition x-ray examination is usually conclusive. We have had no experience with aspiration biopsies, believing that the recognition of malignant disease in such small sections as are available by this method must be inaccurate, even with a good frozen section, it requires a skilled pathologist of long training to make a dependable diagnosis, and in addition one cannot escape the theoretical objection that malignant cells may be transplanted in the tissues outside the prostatic capsule during the withdrawal of the aspiration needle. It is our custom, therefore, to acquaint the patient with the situation, obtain his consent for radical operation, prepare him for this procedure and then expose the suspected area through the usual perineal incision, and to depend entirely on frozen sections taken from this area to confirm the diagnosis in all doubtful cases. This method has been extremely satisfactory, requires only about ten minutes and has proved to be a source of great reassurance to the operator.

The radical operation has been undertaken in too few clinics in this country. Its difficulty has been stressed by some urologists, but any surgeon with thorough training in perineal work and giving sufficient attention to detail can carry it out successfully. This statement is borne out by the fact that successive residents at the Brady Urological Institute have performed this operation successfully on at least a few cases and without a fatality.

The operation requires a somewhat longer time than does prostatectomy for benign hypertrophy, but postoperative shock and hemorrhage, when combated by the usual procedures, can be easily controlled and are negligible factors.

The question of hospital mortality has been raised. Our figure of approximately 6 per cent is not unduly high, and can be favorably compared with mortality figures of operative procedures for the removal of malignant disease in other regions of the body. In our series, at least, postoperative complications have been minimal, and certainly no more prevalent than they are following the operation for benign hypertrophy. The perineal incision heals just as well as in the benign cases,

if not better, while an occasional case of perineal urinary fistula has occurred temporarily, this has healed promptly, and there is no record in any of our cases, which have been followed as completely as possible, of a persistent urinary fistula. In a few cases, stricture at the site of the anastomosis, manifested by diminution in the size and force of the urinary stream, has been noted at subsequent follow-up examination. This condition, however, has always readily responded to simple dilatation.

There has been a widespread impression, among those who are unfamiliar with the radical procedure, that total incontinence is an inevitable result of the operation, and this unwarranted belief has done much to discourage surgeons from performing the operation. One can readily understand how any surgeon would wish to avoid an operation which left his patient totally incontinent, but even if this were the fact, many patients would prefer this condition to undergoing the usual progress of the disease, with its attendant suffering and obstruction.

The question of incontinence depends on the degree of injury to the external sphincter. In some cases where the disease has progressed beyond the apex of the gland into the membranous urethra, for complete eradication of the malignant process a certain degree of damage must be expected and a varying degree of incontinence will result. But if this has not occurred, the membranous urethra may be divided a few millimeters in front of the apex without fear of recurrence at this point, and the external sphincter may be completely preserved. It is obvious, then, that if incontinence does occur, it must be due to injury to the sphincter by sutures placed to complete the anastomosis between the stump of the urethra and the neck of the bladder, and our experience, during the last three years, in the use of sutures placed particularly to avoid constriction of the muscular structures of the sphincter tends to bear out this impression. The anastomosis must, of course, be adequately done, but we have given up the tightly constricting sutures formerly used and have instead adopted three loosely tied mattress stitches, a method devised by one of our former residents, Dr Samuel A. Vest<sup>10</sup> (Fig 1). The lateral sutures are drawn out through the muscles of the perineum and tied there. The anterior suture is placed but is not tied, and one end is tied to a corresponding end of the lateral stitch, which has already been tied. In this way, constriction and actual cutting of the sphincter by the sutures can largely be avoided. Since the adoption of this method, urinary function was found to be ex-

cellent or good in 68 per cent of all cases, although it is only fair to state that many of the patients in whom the older methods of anastomosis were used have attained perfect urinary control.

In the last three years, 34 cases have been operated on, using various modifications of Vest's technique. None of these patients were totally incontinent. In 14 cases (41 per cent), either on dis-

some form of apparatus, although there was no urinary leakage when recumbent. However, certain of these cases have been recently operated on, and there will probably be progressive improvement, in at least some of them with the passage of time and the improvement of the condition of the muscle. Furthermore, in some of the results classified as fair or poor the extension of the dis-

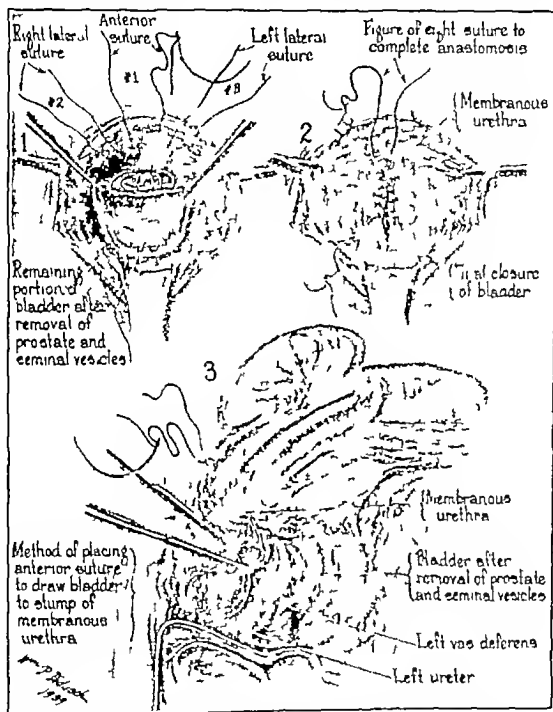


FIGURE 1 The Anastomosis of the Stump of the Membranous Urethra to the Bladder by Means of Three Nonconstricting Mattress Sutures (Vest's technique) Reproduced from *Surgery Gynecology and Obstetrics* (70:935-937 1940) by courtesy of the publisher

charge or follow up, control was excellent and there was no urinary leakage. In 9 cases (26 per cent) control was good, no apparatus was necessary, but the patient complained of the loss of a few drops of urine on coughing, sudden motion and so forth. In 6 cases (18 per cent) control was fair, the patient was partially dependent on some form of apparatus when on his feet, but could go for some hours at a time without leakage. In 5 cases (15 per cent) control was poor the patient when up and about was dependent on

some form of apparatus, although there was no urinary leakage when recumbent. However, certain of these cases have been recently operated on, and there will probably be progressive improvement, in at least some of them with the passage of time and the improvement of the condition of the muscle. Furthermore, in some of the results classified as fair or poor the extension of the dis-

Before discussing the question of ultimate results, a case will be briefly reported which illus-



trates two important points the need of completely removing the seminal vesicles, and the fact that, even if recurrence takes place, it may not interfere with a good functional result

D D M (B U I No 12519), a 51 year-old man, was first seen in June, 1924, complaining of mild obstructive symptoms and terminal hematuria. Physical examination was irrelevant except for slight cardiac hypertrophy and hypertension. On rectal examination, a diagnosis of early carcinoma of the prostate was made, the neoplastic process involving chiefly the right lateral lobe, without extension beyond the apex or into the seminal vesicles. X ray examination showed no evidence of metastases. The sulfonephthalein test and blood urea level were within normal limits.

On July 2, Young's radical operation was carried out under caudal anesthesia. The whole prostate was removed in its capsule, together with the lower two thirds of the seminal vesicles. The latter were soft and there was no gross evidence of invasion, so that the operator did not consider complete removal of these structures as essential.

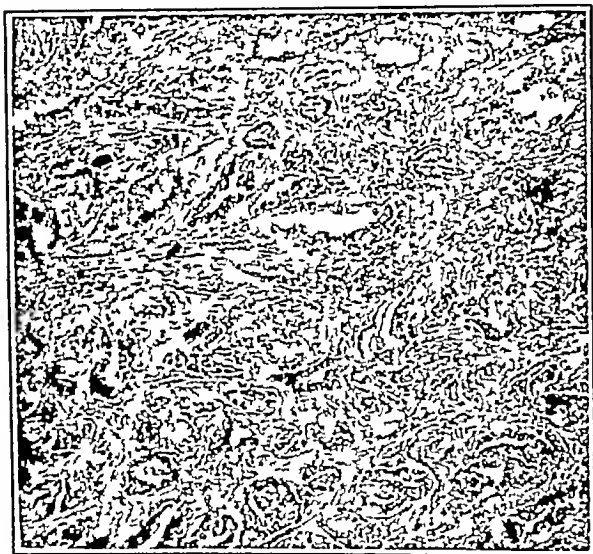


FIGURE 2. Operative Specimen Section showing typical adenocarcinoma of the prostate (low power)

The anastomosis was carried out with three interrupted sutures, uniting the stump of the urethra and external sphincter to the cut edge of the bladder wall distal to the trigone.

Microscopic examination of the operative specimen showed typical adenocarcinoma (Fig 2).

The postoperative course was uneventful, and the patient left the hospital on the 32nd day, voiding without difficulty and with excellent urinary control.

The patient was seen at yearly intervals following operation and remained in excellent condition with a perfect functional result, but on rectal examination an indurated area was noted behind the base of the bladder, which was considered to be scar tissue, as there seemed to be no progressive enlargement of this area. In January, 1928, a cholecystectomy was done for acute cholecystitis, following which postoperative retention occurred and catheterization was necessary for 2 days. Urinary function then again became normal. In 1936, the patient had a definite coro-

nary attack and the blood pressure was found to be 234/178. He died in April, 1939.

A complete autopsy, done at the Billings Hospital, Chicago, showed cardiac hypertrophy and dilatation, coronary sclerosis and healed infarcts of the myocardium. The kidneys, pelves and ureters were essentially normal.

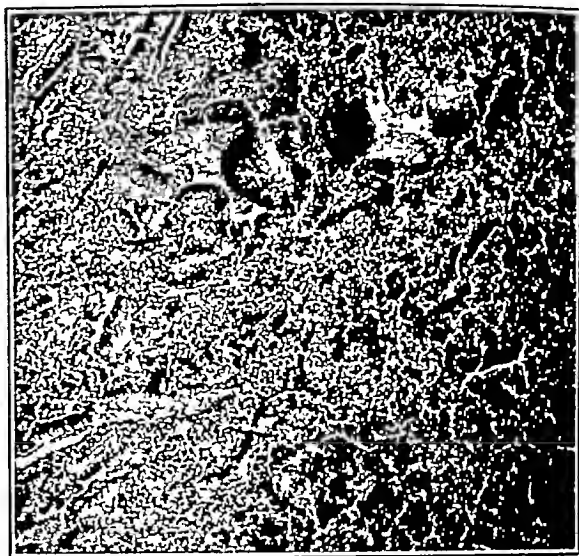


FIGURE 3. Autopsy Specimen Section through retrovesical mass showing extensive carcinomatous invasion (low power)

The bladder was normal except at the trigone, where the mucosa was wrinkled and a puckered, scar like area, with a smooth overlying mucosa, was present. The prostate was absent. Under the bladder, in the region of the upper part of the seminal vesicles, there was a firm mass, 5 by 3 cm, chiefly on the right side, not adherent to the rectum. On section it showed a group of thick walled tubules embedded in scar tissue, and one region showed dilated cystic spaces with reddish and yellowish contents.

Microscopic examination showed the remnants of the vesicles to be thickened and fibrotic, with hyaline and mucoid interstitial changes and vascular sclerosis. The epithelium of the vesicles was relatively normal, although atrophic and desquamated in areas. Throughout the stroma and invading the nerves at the edges were numerous well-differentiated adenocarcinomatous structures (Figs 3 and 4).

This case was considered as cured, and had it not been for the very complete autopsy, it would have remained so classified. It is worthy of note that the tips of the vesicles were not removed at operation, as no gross involvement was demonstrable in the vesicles. It is obvious that tumor tissue must already have been present throughout the vesicles, and the findings in this single case certainly support the contention that in all radical operations the vesicles should be completely removed. It is furthermore extraordinary that the tumor tissue left behind at operation should have grown so slowly, with little or no extension and no demonstrable metastases, over a period of fifteen years. Certainly the original

neoplasm in the prostate, which though circumscribed was fairly extensive, would have progressed to produce obstructive symptoms in this length of time. Smith<sup>11</sup> has contended that the radical operation should be done in suitable cases, even when it is obvious that the disease has extended beyond hope of complete eradication. He has also expressed the view that by complete removal of the prostate and seminal vesicles the main portion of the neoplasm is eradicated, the later development of obstruction is prevented and, in most cases at least, the remaining neoplastic tissue, situated, as it is, high up between the pos-

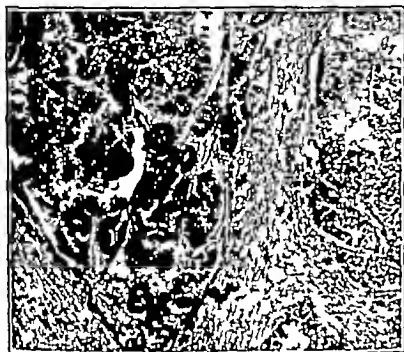


FIGURE 4 Autopsy Specimen Section through tip of seminal vesicle showing invasion by adenocarcinoma similar in type to the neoplasm in the operative specimen (low power)

terior bladder wall and the rectum grows so slowly that it produces no symptoms. Certainly the case cited bears out this contention in every particular. It is our intention to carry out the radical operation in more extensive cases in the future, because we believe that although this patient was never cured of his disease, no other operative procedure or method of treatment could have carried him through fifteen years entirely without symptoms and with such an excellent functional result.

The radical operation for cancer of the prostate has been done in 91 cases, with 6 hospital deaths, an operative mortality of less than 7 per cent. One patient died of surgical shock and hemorrhage, 1 of septicemia following a periurethral abscess, 1, a most unusual case, of cachexia as a result of generalized peritoneal carcinomatosis not recognized preoperatively, and 3 of anuria from ureteral obstruction probably due to tension on the intramural portion of the ureters from the

anastomosing sutures. There was one period in which 26 cases were done without mortality, and another in which 23 operations were performed without a death.

We have been able to follow every patient, with a single exception. There are 44 patients who were operated on five or more years ago. Nine patients died five or more years after leaving the hospital, and were reported by their physicians to have had no evidence of recurrence or metastasis. There are 10 patients living and well, with no clinical evidence of recurrence or metastasis, who were operated on over five years ago. 1 patient is well twenty-five years after operation, 1 thirteen years, 1 twelve years, 1 ten years, 1 nine years, 1 six years and 4 five years.

Among the 43 patients followed five years or more in 5 cases the prognosis was unfavorable before operation and the procedure was undertaken with the idea of removing as much of the malignant tissue as possible, but without the hope of a clinical cure. If these cases are deducted from the 43 which have been followed, there are 38 cases in which the radical operation, with a favorable preoperative prognosis, was done five or more years ago. Of these patients 19 (50 per cent) lived five years or more after operation with out evidence of recurrence or metastasis. Certainly this percentage compares favorably with the results of operative procedures undertaken for the eradication of deep-seated malignant disease in all other regions of the body.

#### SUMMARY

In the last forty years, the orthodox conception of carcinoma of the prostate has been so modified by extensive pathological studies that it is now recognized as one of the most frequent, if not the most frequent, type of malignant disease in men. Clinical cases can be very concisely divided into four groups, in each of which different methods of treatment should be employed. The objective of all treatment should be the preservation as well as possible, of normal urinary function. Suprapubic cystostomy, which was formerly so often used as a routine measure, should be reserved for the occasional case in which operative procedure to preserve urination through the normal channels is contraindicated.

In Group 1 are included those cases with few if any urinary symptoms in which the growth has extended too far for complete radical excision. These should be treated by a combination of radium and deep x-ray therapy.

In Group 2 are included those cases with varying degrees of obstructive symptoms in which the

growth has extended too far for complete radical removal. These are best treated either by transurethral resection of the obstructing tissue or by enucleation through a perineal incision, especially when the carcinomatous process is associated with any degree of benign prostatic hypertrophy. By the latter procedure the major part of the malignant process can usually be removed, any portions that may be left usually grow slowly, and in such a location that there is no recurrence of obstructive phenomena. Transurethral resection used in cases of this type too often results in persistent ulceration and infection and the consequent necessity for repeated operative procedures.

In Group 3 are included those cases which would be suitable for radical operation were it not for the presence of metastases. As in Group 1, these cases are best treated by a combination of radium and x-ray therapy.

In Group 4 are included those cases which are suitable for Young's radical operation. This operation has been carried out in 91 cases with a hospital mortality of less than 7 per cent. Of 38 patients in whom the preoperative prognosis was favorable and who survived the operation, 19 (50 per cent) lived for five years or more after operation. By means of recent improvements in technical details, especially in methods of suturing designed to complete the anastomosis between the stump of the urethra and the neck of the bladder without injury to the external sphincter, urinary function was found to be excellent or good in 68 per cent of cases.

These facts should be sufficient to impress the general medical profession that if carcinoma of the prostate can be recognized before it has progressed too far, an operative procedure with good functional results is available which will offer a five-year clinical cure in approximately 50 per cent of the cases. All clinicians—medical, surgical and urological—should therefore be stimulated to recognize this disease in its early stages while hope of complete removal is still present.

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#### DISCUSSION

DR. GEORGE G SMITH, Boston. I have been doing this operation for some time and the only guide I had was the excellent description in Dr Young's book. I have never seen one of these operations as it is done in Baltimore, and consequently I was very much interested in the pictures Dr Colston showed. I should like to ask about the closure of the bladder neck. I have brought the mid point of the trigone to the urethra and sutured it. The results in 71 cases I have operated on in the last twenty years have been singularly parallel to those of Dr Colston. There have been five hospital deaths, but in the last 50 cases only one, that of a man of eighty-four who died of shock. All the patients who died were men over seventy-five, so that as a general rule I do not perform this operation on men over that age. With transurethral resection they can be made comfortable. Of these 71 patients, 29 died of the disease after having lived an average period of three years. Five were well for five to nine years.

Recurrences were found in 30 of these cases. Including living patients, they were as follows: local recurrence, 12 cases; carcinomatosis, 1 case; metastases in the bones, 3 cases; metastases in the lungs, 1 case; metastases in the spine alone, 7 cases; local recurrence and metastases in the spine, 6 cases. Nine patients died of other causes, 4 lived for at least five years, the longest survival being nine years, none had signs of carcinoma. There are 4 patients alive with recurrences, the postoperative years being eight, seven, four and a half and four. Twenty-one patients are alive and apparently well, 3 of these for at least ten years postoperatively, and 4 between five and ten years. The others were all operated on less than five years ago, so that statistics are lacking. Seventeen patients have enjoyed perfectly good health for at least five years after operation.

The control of urination was poor in 6 cases, 2 of these patients had tabes dorsalis, while 1 had cerebral thrombosis and was feeble-minded and so could not control urination. Three patients had fair control, and 62 good to perfect control, the leakage consisting of a few drops on coughing, sneezing or other exertion. I believe that this operation is decidedly worth while. Hardly any patients developed retention of urine. There has been little difficulty with stricture at the bladder neck and urethra, and this can be remedied by occasional dilatation.

Dr Colston and Dr Young have done the major work on this operation, and I hope that more surgeons will take it up. I do not agree with the many writers who hold that by the time one can make the diagnosis it is too late. Many physicians have detected carcinoma of the prostate and sent patients to me, and they have been right in their diagnoses. Anyone who can feel the hard area in the prostate can make the tentative diagnosis.

DR. CLYDE L. DEMING, New Haven, Connecticut. We in the state of Connecticut have recently become interested in carcinoma of the prostate and in its relative frequency. Last spring a symposium was held on this disease, and the Yale University Health Department was asked to estimate the number of possible cases in Con-

rectect. Taking the figures of autopsies and reports in the literature as a basis, it reached an estimate of 25,000, and as this looked too high it cut the figure in two before presenting it. In any event, the estimate shows that the frequency of this disease is outstanding. Since Connecticut as well as other states is encouraging clinics and evincing an interest in malignant diseases we should make some attempt to cure carcinoma of the prostate.

What is being done toward this end, and how many clinics are making an endeavor to cure this form of malignancy? I have done a number of radical operations. One patient is comfortable in his fourteenth postoperative year several in their sixth year none show recurrences. I have always been, and still am, inclined to operate to cure this disease, wherever possible. The question arises in obstructive cases without bone metastases as to the better type of operation—a conservative perineal operation which gives satisfactory results so far as relief is concerned, or transurethral resection. The membranous urethra is sometimes invaded, but often not. The mucous membrane prevents growth into the urethra and is, hence, protective. If we remove it by transurethral resection, we leave an open carcinomatous wound. Comparing the perineal operation with transurethral resection has made me dissatisfied with the latter because the patients void purulent urine as long as they live. Transurethral resection is not acceptable as a means of relieving carcinoma of the prostate with complete obstruction for it does nothing to effect a cure. It is time for us to play our part and make an attempt to cure some of these cases.

Dr. GRASBOM J. THOMPSON Rochester Minnesota We are all interested in the cure of cancer. Dr. Colston has called your attention to the fact that he selects for the radical operation only a small proportion of the cases that he is called on to treat, certainly less than 10 per cent. This low percentage should not discourage those who are inclined to be pessimistic, since this operation affords the hope of cure. Short of cure, one can accomplish a great deal in the relief of the patient.

Dr. Smith has stressed the fact that subtotal removal of the carcinomatous prostate accomplishes a great deal. There is a lot to be said for the operation radical or subtotal in the face of an apparently incurable condition. I am sure that at Rochester we have not in the past been attacking this problem so optimistically as we should have, and we shall look forward to improvement in our attitude. But in the last ten years, through the operation of transurethral resection we have accomplished for many patients relief of the symptoms, and that accomplishment has been very much worth while. In spite of the fact that there need be repetition of the operation before the patient's death we can adequately relieve the obstructive symptoms. That is something we should not lose sight of in the discussion of the radical operation. Granted that it is a wonderful operation it is certainly a fact, unfortunately that carcinomas of the prostate do not produce symptoms calling the attention of the patient or physician to it early enough. Examination of any old man is not complete unless it includes a rectal examination for carcinoma of the prostate. Let us stress that fact, and hope to accomplish cures by the operation that Dr. Colston has described this evening.

Dr. SAMM I should like to ask Dr. Thompson whether he uses any other method, such as radium or x-ray treatment.

Dr. THOMPSON We use many other methods. We employed in the past the perineal implantation of radium seeds in a series of cases we have used extensive deep

x-ray therapy in far more cases. The final results are still uncertain. I recall a number of patients who gained relief for seven or eight years. I recently operated on a man of eighty-three on whom I had performed a resection seven years previously. He developed symptoms of obstruction and I resected more tissue, and he again has what he regards as normal urinary function. Enlarging upon that fact, I disagree with the many surgeons who hold that results over a term of years cannot be regarded as satisfactory unless purulent urine and similar symptoms have been adequately controlled. Certainly we are interested in relieving patients of other discomforts, and resection restores the urine to an entirely normal status in a large proportion of cases.

Dr. RALPH H. JENKINS, New Haven Connecticut What is the true indication for a radical perineal prostatectomy? You described a case, as I remember the particulars in which the carcinoma of the prostate began in the lateral lobe and spread to the vesicle. If it is over the vesicle then it is outside the capsule.

Dr. FLETCHER H. COLBY Boston The early radical removal of the prostate is a splendid idea but very few cases are suitable for the operation. Perhaps seven a year come to the Massachusetts General Hospital. However this procedure represents a fair attempt to cure cancer. I have performed the operation only five or six times so that I am not so familiar with it as are others. It should be attended with a low mortality and moderately good but not complete urinary control. Its ability to effect a cure is uncertain.

As regards the treatment of cancer by irradiation our three years' experience at the Huntington Memorial Hospital has shown rather poor results so far as the radio-sensitivity of carcinoma of the prostate is concerned. The large majority of cases suitable for irradiation have shown little or no response. Large doses amounting to 8000 to 16,000 r are given. The patients have stood the exposure well, but the prostatic tumors have not shown the same degree of radio-sensitivity as have others. Only 1 patient has responded well. He presented himself with complete retention a year and a half ago, and transurethral resection was performed. He was then given three courses with the supervoltage machine. I doubt if anyone here would now recognize him as having cancer of the prostate.

Dr. WILLIAM C. QUINBY Boston Some of the variation in the attitude toward the treatment of carcinoma of the prostate is undoubtedly influenced by the facilities at the disposal of varying clinics. When radium first appeared we were hopeful that great results would be forthcoming in the treatment of carcinoma of the prostate as well as that of the bladder. Unfortunately however the results have been disappointing on the whole. Treatment by high-voltage x-ray has also been employed extensively in those clinics in which suitable apparatus was available. Definite progress, it is thought, is being made in the control of not the cure of prostatic carcinoma by this newer modification of x-ray but thus far it would seem in spite of a few cases,—one of which was reported by Dr. Colby—that this method also cannot be relied on. An occasional patient is found whose tumor is definitely responsive to high-voltage x-ray and after treatment the growth seems to disappear entirely. I have seen one such patient whose prostate after extensive radiation became apparently normal on physical examination. At the end of about three years however the cancer recurred.

To my mind transurethral attack on a carcinomatous prostate is of no value except to relieve obstruction to the

bladder There is also considerable evidence that a partial removal of a carcinomatous prostate by this method causes the remaining malignant tissue to take on an increased rate of growth There is no doubt that transurethral resection aids some patients with carcinoma of the prostate, but in these it is my opinion that the material that is removed is merely benign hyperplastic tissue which overlies the carcinoma

Dr Thompson's presence recalls a remark by Dr William J Mayo several years ago, 'If a surgeon in his fight against cancer has not about a 10 per cent mortality, he is not fighting the disease hard enough' This opinion, made by a very wise and shrewd individual, I think we should all take to heart.

If, by the ingenious operation that Dr Colston has shown us, 91 patients can undergo total prostatectomy with only 6 fatalities, 3 of which were remediable, this operation has a great deal in its favor

There is no doubt that thoroughly trained surgeons are leaning more and more toward total prostatectomy for carcinoma, being disappointed by the effects of such agencies as x ray and radium It must always be remembered that in one out of every five cases with urinary obstruction the condition is due to cancer We must fight this

Can Dr Colston tell us what percentage of the total group of patients having carcinoma of the prostate these 91 patients comprised, and in the other groups, what forms of treatment he advocates?

DR E GRANVILLE CRABTREE, Boston Among the pleasures that come to those in the medical profession are the cases, often too few, in which a surgical procedure brings to the patient a long and useful life. One of my patients has arrived at the age of ninety two without ever knowing he has had total resection of the type that Dr Colston has mentioned, and has shown no sign of recurrence. I have not had good luck with my other cases. Nine of them were too advanced. There have been 3 of eight years' duration and 2 between five and six years

DR COLSTON (closing) I appreciate the stimulating discussion that has been carried on As regards Dr Smith's point about bringing the trigone down to the urethra, this procedure might be very valuable I shall try it, for it may stop the constriction of the ureters responsible for most of our deaths I am glad that Dr Smith stressed the matters of age and life expectancy To those who encounter failure, one reason for it is too large a carcinoma, and the other too old a patient.

Dr Demings' figures are alarming, since they run into

the thousands But they are probably conservative, as judged by the results of the pathological investigations of Rich, and of Moore in Vienna I agree with Dr Deming as regards the cases in which there is a considerable amount of benign hypertrophy associated with carcinoma. Better results are achieved by perineal prostatectomy, with the removal of as much tissue as possible

In reply to Dr Thompson, there are certain types of cases that are suitable for transurethral resection, especially where the process has extended beyond hope of radical cure and planes of cleavage will not open.

In answer to Dr Jenkins's question about the indications for the radical operation as I said, the case reported undoubtedly had carcinoma in the lymphatics outside the capsule, although we did not know that to be so. The operation is indicated when the growth is confined within the capsule, as ascertained by rectal examination, and has not extended into the membranous urethra, even though the bases of the vesicles are involved, if other conditions, such as I have outlined, are satisfactory, a case of this kind should be given the benefit of the operation in the hope of curing the patient, or of preventing recurrence where the growth is cut off from the lymphatics.

Dr Colby is quite right in saying that the fact that we see so few cases is a tragedy I do not see how this can be remedied except by the co-operation of physicians, and their training themselves to suspect any hard nodule that they feel on rectal examination Very few physicians fail to make such an examination in patients over fifty, yet even so very few cases are seen by the urologist. I was interested in Dr Colby's belief that the radio-sensitivity is slight, but occasionally one sees a treated case where the diagnosis can scarcely be made Application of radium through the rectum has been condemned, but we do it occasionally In a few cases malignancy has been reduced to such a degree that diagnosis, without having seen the patients previously, could not have been made.

Dr Quinby asked what percentage these 91 cases represent of the total number, that would be hard to say, but Dr Thompson is right. I believe that of all the cases treated over a period of fifteen years, only 4 or 5 per cent were suitable for radical operation, which is of course discouraging Dr Quinby also asked what treatment is used when radical operation is not indicated. If there are no obstructive symptoms, we give surface applications of radium, and sometimes we use x ray in the hope that in the occasional case the growth may be stopped In cases with urinary symptoms we use transurethral resection or perineal prostatectomy, depending on the indications

## RIBOFLAVIN DEFICIENCY\*

## Report of a Case in a Child with Cure by Specific Treatment

WILLIAM P. SHIELDS, M.D.†

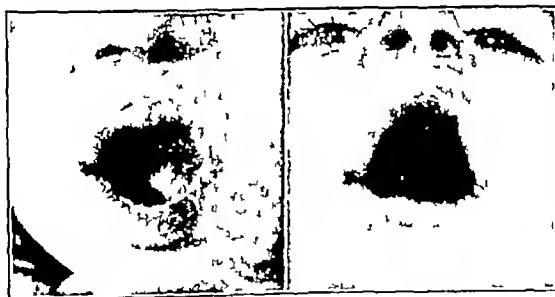
PROVIDENCE, RHODE ISLAND

**R**IBOFLAVIN deficiency as evidenced by cheilosis is new in the category of vitamin B deficiencies. Stannus,<sup>1</sup> in 1910, noted lesions on the lips which he linked with pellagra and its associated food deficiencies. Sebrell and Butler<sup>2</sup> were able to produce these lesions in a number of patients on a diet poor in riboflavin, and to cause their disappearance by the administration of synthetic riboflavin. Oden, Oden and Sebrell<sup>3</sup> and Sydenstricker, Geeslin, Templeton and Weaver<sup>4</sup> report clinical cases in Georgia that were cured by specific therapy. More recently, Jolliffe, Fein and Rosenblum<sup>5</sup> have noted the occurrence of this entity in New York City. Practically all their cases showed manifestations of other deficiency diseases, such as pellagra, scurvy

Treatment consisted of 1 tablet of Feosol twice daily, 1 ounce of tomato juice daily and instructions to increase the diet in respect to milk, fruits, vegetables and meats.

The patient was seen again at the clinic on September 26 and 1 teaspoonful of cod-liver oil three times daily and a 6-gr tablet of brewers' yeast (Squibb) three times daily were ordered. There were no apparent skin lesions. At a third examination on December 9 a diagnosis of impingement of the lips was made and the local application of a 2 per cent aqueous solution of gentian violet was advised. The next visit to the clinic was on January 2, 1940 when lesions centered about the nose and lips were noted, which according to the mother had been present since the previous October. The patient had the appearance of a healthy fairly well-nourished child and the only complaint was anorexia.

The diet of the family was restricted because of a limited income, \$6.00 a week being expended for food for the family of six. Meat was served once a week, a quart



A

B

FIGURE 1 Before Treatment

and polyneuritis, and many had alcoholism as a basis.

## CASE REPORT

A 6-year-old girl of Italian descent was first seen at a clinic for children in Providence, Rhode Island, on September 19, 1939. She had no appetite and was slightly underweight. She had been born prematurely and had had no cod liver oil or orange juice since birth. She appeared healthy and the physical examination was negative except for moderate pallor of the mucous membranes. The clinical diagnosis was slight malnutrition, with possible anemia.

of milk was bought daily and was apportioned among all the members of the family. The diet consisted principally of starchy foods, namely macaroni and potatoes. Fruits and vegetables were obtained only occasionally. The patient was the only one in the family to develop specific lesions.

The average daily diet was as follows:

Breakfast: coffee and milk, crackers.

Dinner: mostly macaroni mixed with beans and peas on alternate days; white bread in large quantities; potatoes occasionally; no other vegetables; no meat except on Sundays, usually in the form of meat balls; chicken very occasionally; no lamb or steak; no fruits; total milk ingested was about a glassful a week.

Supper: leftovers from the noonday meal together with an occasional egg.

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The lesions were ulcerating in character and involved the upper and lower lips, together with deep transverse fissures at the angles of the mouth, not including the buccal mucosa. The lesions on the lips proper were at the line of closure, and were covered with a crust which on removal left a bleeding surface. The lips themselves were not sore or inflamed, nor was there any swelling. The nasal involvement consisted of a fine, scaly desquamation at the mucocutaneous junction on the ala nasi. There was also a mild progression into the vestibule, with crust formation. Physical examination was otherwise negative.

Because of the similarity of the symptoms to those in recently published reports, mentioned above, a diagnosis of vitamin B<sub>2</sub> (riboflavin) deficiency was entertained. Synthetic vitamin B<sub>2</sub> was the sole therapy applied. One mg of Flavaxin (Winthrop) was given subcutaneously on January 4 and again on January 5. Some improvement

graphs shown in Figure 2 were taken at this time.

Riboflavin was then given in the dose of 0.5 mg daily until February 13, when it was replaced by 4 gr of Tabloid Yeast Concentrate (Burroughs Wellcome & Co.), four times daily.

When last seen, the patient's appetite was still not very good but was improving. There were no other complaints. The family diet was being supervised by social agencies to ensure the presence of all essential foodstuffs.

### SUMMARY AND CONCLUSIONS

A case is reported of a child who presented lesions about the nose and lips similar to those described by others<sup>2-5</sup> as being due to a deficiency of vitamin B<sub>2</sub> (riboflavin). The diet was inadequate, and was particularly lacking in the



FIGURE 2 After Treatment

was noted, so that 2 mg was given on January 6, with continued improvement on January 7, but on January 8 there was complete recrudescence of the lesions. At this time the photographs shown in Figure 1 were taken. In accordance with the therapy of Sydenstricker and his associates,<sup>4</sup> larger doses were given, and because of the ease of administration the oral method was selected. Riboflavin (Abbott) was given in doses of 15 mg daily for 3 days. Two days from the beginning of the oral dosage there was complete resolution, with the exception of a slight persistence of the fissure at the angle of the mouth on the right. This showed a healthy, healing surface. Thereafter, 10 mg of riboflavin was given for 3 days. On January 18, 3 days after the discontinuance of the drug, the lips showed signs of a relapse. How much of this was due to exposure to cold was hard to determine, so that it was decided to postpone any decision as to the cause. On January 20, this disturbance had increased considerably. It appeared that there was a recurrence, there was a superficial desquamation of the mucosa of the lips at their place of closure, accompanied by linear cracks. The fissure was more marked at the right angle of the mouth. Three milligrams of riboflavin was given daily by mouth for 8 days, and when the patient was seen on January 30 there was complete healing, including the fissure at the right angle of the mouth. The photo-

graphs shown in Figure 2 were taken at this time.

There have been no reports of this condition in childhood. Significant also is the fact that the reported case was unaccompanied by any other manifest food deficiency, and that it developed in an urban center of New England, in a member of a family in the low-income group. Very likely this condition is not unusual in such groups, where the diet is inadequate because of economic factors.

I am indebted to Mr C Wallace Bohrer and Mr Thomas B Casey, of the Rhode Island Department of Health, for the photographs.

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# ERYTHEMA MULTIFORME BULLOSUM WITH INVOLVEMENT OF THE MUCOUS MEMBRANES OF THE EYES AND MOUTH (STEVENS—JOHNSON DISEASE)

## Report of a Case

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THE scarcity of case reports of erythema multiforme bullosum with eye and mouth involvement prompts the addition of another to the list.

### CASE REPORT

A 4-year-old white girl was admitted to the Lincoln Hospital because of diffuse skin lesions and fever of 3 days duration. The family history was irrelevant, and the patient's development was normal. Except for measles, which she had had at the age of 3 there had been no other

but no chills. Except for the tincture of larkspur and the hair lotion, no medication had been used either externally or internally.

On admission the patient was acutely ill and obviously in great distress (Figs. 1 and 2). Exclusive of the scalp the skin of the entire body was covered with a confluent erythematous maculopapular eruption. The upper extremities, face, neck and chest anteriorly were covered with bullous vesicles ranging from the size of a pinhead to an area 7 by 15 cm. Some of the bullae had ruptured, exuding a thin watery fluid. Where the skin had desquamated, a raw red oozing surface was visible. Where there were no bullae the affected skin could easily be rubbed off. The posterior portion of the thorax was the least involved. The scalp was free of lesions, the hair border



FIGURE 1

*This photograph shows the distribution of the skin lesions on the trunk and upper extremities at the time of admission. Note the large exuding areas on the dorsums of the forearms where the bullae had ruptured.*

childhood diseases. She complained of frequent sore throats and colds, especially in the winter. She had had discharge from both ears for 5 weeks ending 3 weeks prior to admission. She was in apparent good health until the onset of the present illness, 3 days before admission. On that day she had a haircut. The barber used a hair lotion and that evening her mother put some tincture of larkspur on the child's hair. She became nervous that night, and was feverish. The next morning the face was diffusely reddened and the eyes were injected. During the day the erythema spread to the neck and shoulders; in 2 days it completely covered the body. On the day before admission, large bullae formed on the arms, face and upper part of the body. In some places these ruptured. The patient complained of intense pain on micturition. She had fever



FIGURE 2

*In this photograph taken on admission note the expression of discomfort, the glutinous serous exudate and the crusting about the lips and nose. Neither eyelid could be opened because of thick, yellow exudate.*

acting as a line of demarcation. The eyelids could not be opened because of a thick, yellow purulent exudate. The skin of both ears was entirely denuded. The right eardrum was thick and scarred, the left eardrum was dull and the light reflex was absent. Breathing was difficult because of a thick, mucoid secretion to the nose. The lips were raw and covered with large, white, ulcerated patches. The tonsils were not involved. The rest of the physical examination was negative.

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The diagnosis on admission was pemphigus and bilateral, subsiding, acute suppurative otitis media. Two members of the visiting staff, Dr. Peter Vogel and Dr. Charles Marrin, saw the patient the next day and thought the case similar to those described by Stevens and Johnson<sup>1</sup> in 1922 and by others<sup>2-7</sup> since then, and designated by them as eruptive fever with stomatitis and ophthalmia.

The patient was placed on a course of Neoprontosil,

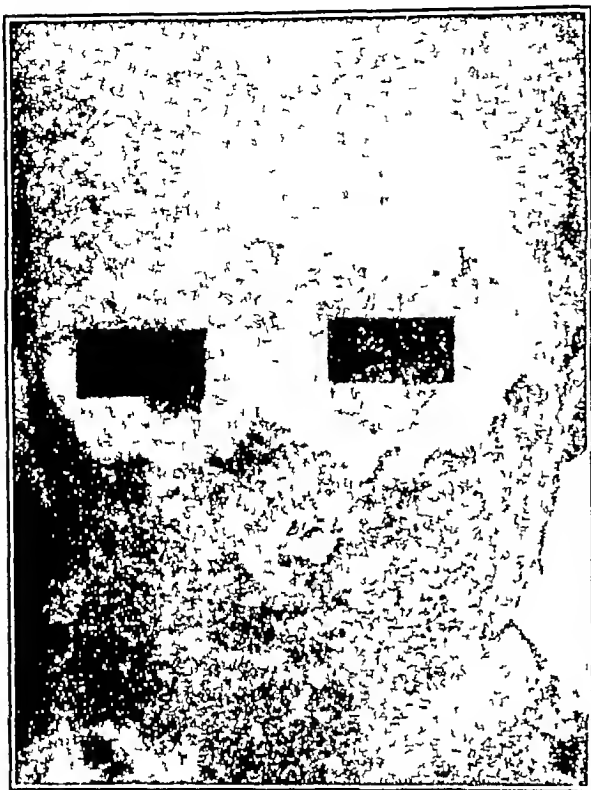


FIGURE 3

*Note the marked bilateral ectropion caused by the thick scab formation after ten days of treatment*

40 gr a day for 9 days, frequent boric acid eye washes and applications of 1 per cent gentian violet to the skin lesions. Because adequate food and fluid intake could not be provided, a continuous infusion of 5 per cent glucose in saline solution was given for 3 days in order to maintain the fluid requirement. Several drops of a 1:2500 solution of Metaphen were instilled into the eyes three times a day, and later on Butyn Metaphen ointment was used. Eighteen hundred milligrams of vitamin B and 25 mg. of vitamin C were administered daily. Sedatives were given liberally.

In the course of 2 days the patient was able to open her eyes. It was then observed that the corneas were intact. Seven days after onset the discharge from the eyes was noticeably decreased. Vision was unimpaired at all times. Thirteen days after onset a cicatricial ectropion developed, due to scab formation under both lower lids (Fig. 3). The corneas were thus partially exposed during sleep, and it was feared that corneal scarring might occur. The scabs were therefore softened and removed, and in another 10 days there was almost complete restoration of the eyelids to normal. By the 18th day after onset a moderate degree of photophobia was evident. This was relieved by the wearing of smoked glasses, and by the 21st day the eye condition was considered normal.

The bullae were confined to the upper portion of the body. These and other desquamated areas responded well to gentian violet and starch baths. By the 11th day the skin lesions had assumed a brownish tinge and scaly appearance, leaving the denuded areas dry. The face was covered with a hard, dry crust. The mouth and lips bled easily. The scalp was not involved primarily, but on the 18th day a small lesion the size of a quarter was noted over the occiput. It was believed to have been caused by pressure and was unlike the other skin lesions. By about this time the skin lesions had healed almost completely, and three fourths of the scabs had fallen off or been removed. On the 18th day, small, nontender vesicles appeared on the palms of the hands, and in a few days the superficial layers of skin there came off. A few days later the same lesions occurred on the plantar surfaces of the feet. No scars remained on any portion of the body (Fig. 4).

The temperature on admission was 102.2°F. In 3 days it had reached a peak of 104.8°F. It then dropped slowly,



FIGURE 4

*In this photograph, taken on discharge from the hospital, faintly pigmented areas are the only remaining evidences of the lesion*

reaching normal by the 14th day after onset, and continuing normal until discharge. The urine on admission had a trace of albumin with many red blood cells, but the specimen was not a catheterized one, so that it was believed that this was a contamination due to severe vaginal lesions. Subsequent specimens of urine were clear. On admission the hemoglobin was 11.2 gm., the red-cell count 3,870,000 and the white-cell count 8750, with 53 per cent polymorphonuclears, 43 per cent lymphocytes and 4 per cent mononuclears. On the 8th day after onset the white-cell count was 14,600, with 56 per cent polymorphonuclears, 40 per cent lymphocytes and 3 per cent

mononuclears. On the 20th day it was 20 400 with 75 per cent polymorphonuclears, 20 per cent lymphocytes and 5 per cent mononuclears. A Wassermann test was negative, and the blood-urea-nitrogen and blood-sugar levels were normal. A culture from the mouth yielded *Staphylococcus aureus* and one from the conjunctiva *S. aureus* and *S. albus*. A guaiac test for blood in the stool on admission was positive. A biopsy specimen taken of one of the skin lesions 2 weeks after onset showed a mild, nonspecific inflammation of the skin.

Stevens and Johnson<sup>1</sup> in 1922 described this syndrome as that of an eruptive fever with stomatitis and ophthalmia. Other cases have since been reported,<sup>2-7</sup> in almost all of which the average length of time for resolution of the skin lesions was eighteen to twenty-one days. There were practically no complaints of pain or of itching, and the scalp was free of lesions. In 3 of the reported cases there was formation of bullae. A few of the cases showed leukopenia. In the 9 cases described only 2 patients escaped total blindness, and these remained partially blind. Dr John M. Wheeler of the hospital staff suggested that effective eye treatment was the only urgent need, and attention was focused on this procedure.

Of all cases described, only 1, exclusive of ours, occurred in a girl, the ages ranged from twenty-two months to sixteen years.

It is doubtful whether Neoprontosil was of any value in the treatment of this case, although it may have acted as a prophylactic against secondary infection. In the case reported by Chuck and Witzberger<sup>6</sup> the condition was accompanied by an oral Vincent's infection; the authors suggest

that cases of exudative erythema multiforme reported previously might have a similar etiology and, further, that, if their contention is correct, it would seem logical to employ spirocheticidal therapy.

In another case, that of Edgar and Syverton,<sup>7</sup> a skin biopsy was performed, but nothing of note was reported.

#### SUMMARY

A case considered to be one of erythema multiforme bullosum with involvement of the eyes and mouth, and with complete resolution of the skin lesions in less than three weeks, is reported.

The essential features were lack of involvement of the scalp, involvement of the mucous membranes of the eyes, mouth and vagina, an acute course, lasting less than three weeks, a moderate leukopenia during the first few days of the illness and absence of scar formation after healing of the skin lesions.

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REPORT ON MEDICAL PROGRESS

PHARMACOLOGY

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IT WAS my purpose to devote this year's report to a consideration of the toxicity of various drugs in the human subject. The reports of such poisonings are, however, so often incomplete from the pharmacological point of view, especially so far as dosage is concerned, that the original plan had to be abandoned. Necessarily, details of dosage are often lacking since most poisonings are accidental or suicidal, but approximations could often be obtained. This prompts the suggestion that either federal or state agencies or both be set up to collect and collate the reports of violent deaths, and that these figures be studied in order to gain an accurate idea of the lethal doses of various poisons in man, and the relation of these doses to those of the same drugs in other species. In this way a large amount of data could be rapidly accumulated.

The last available publication of the Bureau

TABLE 1 Deaths from Poisoning in the United States (1937)

POISONOUS AGENT	SUICIDAL		ACCIDENTAL		TOTAL	
	NO OF DEATHS	PER CENT	NO OF DEATHS	PER CENT	NO OF DEATHS	PER CENT
Gas	2552	46.5	1704	53.5	4256	49.1
Non volatile poisons	2933	53.5	1482	46.5	4415	50.9
Carbolic acid*		17.2		2.9		6.3
Cresol		14.3		3.0		5.4
Strychnine (nux vomica)		11.6		8.4		5.3
Mercury		10.4		5.0		4.4
Cyanides		9.2		—		3.1
Arsenic		8.0		5.3		3.6
Barbiturates		7.5		13.2		4.8
Narcotics		1.1		2.0		0.7
Nicotine		1.1		1.0		0.5
Lye		0.3		10.0		2.8
Totals	5485		3186		8671	

\*Only the more important agents are listed and the percentages relative to all deaths from non volatile poisons

of the Census<sup>1</sup> shows that violent and accidental deaths occurred in 1937 at the rate of 104 per 100,000 population. These were distributed as follows: homicide, 76; suicide, 149 (by poison 43), accidental, 81.5 (by poison 24). Thus, 6 per cent of the total deaths were due to poisons, and of these, about half were from gas. The kind of poison used for suicide and involved in accidental death is of some interest, hence, Table 1 has been compiled.

These figures are of particular interest in showing the importance of accidental poisoning by

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barbiturates. This is further emphasized by the fact that deaths from barbiturates, both suicidal and accidental, doubled within the five years ending with 1937. Research on the therapy of poisoning with these drugs has engaged the attention of many American laboratories. Treatment by various analeptics was given great impetus some years ago by the study of picrotoxin by Tatum and his co-workers.<sup>2</sup> Immediately other analeptics were tried, and the relative value of the various drugs has since been a subject of active discussion. Naturally, this has led to a study of the details of action of these drugs, and also to the use of certain stimulant sympathomimetic drugs in conditions of depression. Chakravarti<sup>3</sup> has studied very thoroughly the comparative action of Cardiazol, Coramine, strychnine, picrotoxin, amphetamine (Benzedrine) and ephedrine. Careful studies on mice showed the order of toxicity to be strychnine, picrotoxin, Cardiazol, amphetamine, Coramine and ephedrine. This was compared with the "maximum human therapeutic dose." Chakravarti fails to tell how this was determined, and certain of the figures for this dose are decidedly too low. Of more utility is the comparison of these drugs as awakening agents when used on mice narcotized with pentobarbital. The order of potency in these experiments was amphetamine, Cardiazol, picrotoxin, strychnine, Coramine and ephedrine. To test the antidotal action, a dose of Nembutal calculated to kill 78 per cent of the animals was injected intraperitoneally, simultaneously with one or two lethal doses of the analeptic. Under these circumstances, only picrotoxin and Cardiazol showed any life saving action. In addition, the medullary action of these drugs was studied in various animals, and in relation to the lethal dose, only ephedrine and amphetamine were found to have any significant action as respiratory stimulants. None had any valuable action on the medullary vasomotor center, and augmented the carotid-sinus reflex only when given in very large doses. Chakravarti concludes that picrotoxin and Cardiazol are the only drugs that antagonize the toxic action of pentobarbital. Dille and Hazelton<sup>4</sup> call attention to the secondary depression that has been observed after the use of analeptics in barbiturate

poisoning in human beings, and studied picrotoxin and Metrazol in this connection. They point out that cortical depression in rats and rabbits is independent of the convulsive dose and may, indeed, precede it. This occurs also with Metrazol, but is distinctly less with picrotoxin. Convulsive doses of Coramine, cocaine, caffeine and amphetamine do not produce similar depression.

Of great importance in the study of analeptics is their fate in the body. The effectiveness of picrotoxin, for example, in combating the effects of Nembutal poisoning is not susceptible of intelligent practical application unless we know the rate and mode of disposal of the injected drug. Duff and Dille<sup>2</sup> have supplied data on this point. They injected large doses—5 mg. per kilogram of body weight—of picrotoxin into dogs and rabbits and killed the animals at various stages of the poisoning. Convulsions were controlled by pentobarbital or ether. It is evident from this work that the drug rapidly disappears from the blood and appears in liver and skeletal muscle, where it is apparently largely destroyed, since only traces are found in the urine. Two hours after injection less than 0.02 mg. per 100 cc. of blood could be demonstrated. This study explains the clinical observation that repeated doses of picrotoxin are necessary to combat barbiturate poisoning since the analeptic action evidently depends on maintaining a definite blood concentration in order to obtain the continuous effect on the central nervous system that is desired.

An ingenious method of comparing the potency of analgetic drugs was devised by Pfeiffer<sup>3</sup> who studied their effect on hibernation. It was found that vasoconstrictor drugs were much better tolerated than convulsive drugs. Spinal convulsions were poorly tolerated in the extreme acidosis of hibernation. However, both Metrazol and picrotoxin had good analeptic indices against the hibernating state, and the former showed no increased toxicity in the hibernating animal as did the other convulsant drugs, especially the spinal convulsants. Cocaine showed no increase in toxicity in these acidotic animals and proved to be so efficient as an analeptic that these authors suggest its inclusion in this group.

The analeptic activity of sympathomimetic substances has justly received increasing attention. Tainter and his co-workers<sup>4</sup> have been very active in studying the relation between chemical constitution and physiologic action in this group of drugs, and have undertaken a comparison of their activity in counteracting deep narcosis produced by chloral hydrate, tribromethanol in amylene hydrate (Avertin) and pentobarbital in rats. The

return of three sets of reflexes—abolished by the narcosis—after the injection of the stimulant were used as criteria of the potency of the drug, these were the righting reflex, which requires coordinated muscular and vestibular movements of a relatively high order, the corneal reflex, which principally involves cephalic pathways, and electrical stimulation of the ankle, with muscular response proximal to the point of stimulation, spinal paths thus being involved. Of the twenty-two amines studied, half showed no analeptic activity. The remainder were compared with analeptics of the convulsant group. Several seemed to show stimulant effects on one of the reflexes studied while increasing the depression of the others. Similarly different responses were obtained depending on the depressant used. Metrazol did not hasten recovery from the effects of Avertin, though it did from those of chloral. The most effective stimulants were Cobefrine, 1-pseudo-ephedrine and phecol 2 amino-1-propane. These have nothing in common in their chemical structure that could be connected with their analeptic efficiency. The investigators further compared the analeptic potency with power to raise blood pressure, but found no relation between these two properties. This finding agrees with that of other investigators.<sup>5,6</sup> Under the conditions of this experiment, caffeine, Coramine, picrotoxin and amphetamine were ineffective against Avertin, and in addition, the last, in large doses, delayed recovery. Amphetamine was effective in hastening recovery of the righting reflex only against chloral and pentobarbital. The selectivity of action seen in these experiments suggests the need for further detailed work in order that the optimum analeptic for any given depression may be used.

In this connection the observation of Orth, Leigh Mellish and Stutzman<sup>10</sup> as to the superiority of Neosynephrine as a stimulant in cyclopropane, ether and chloroform narcosis is of importance. Their study was initiated by the observation that these volatile anesthetics sensitized the heart to adrenalin, as shown by the appearance of arrhythmias when the drug was injected during narcosis. Various members of the group related to epinephrine were studied and it was found that Neosynephrine was the least apt to produce arrhythmia.

Just as the disposal of picrotoxin is of importance to its use as an analeptic, so is that of the long-acting sympathomimetic drugs. The timely investigations of Beyer and Skinner<sup>11</sup> throw some light on this subject, at least in relation to amphetamine. These authors describe a method for the detection and determination of the drug,

they found that somewhat less than half was excreted in the urine within forty-eight hours following ingestion. The percentage of a given dose excreted generally paralleled urinary volume, but was greater when the small doses were administered. It was shown that all the drug is absorbed from the gastrointestinal tract, and it is obvious from the fact that the drug excretion so markedly outlasts its physiological effect that it is partly inactivated by a loose combination with some agent in the body. This inactivation apparently takes place largely in the liver, since animals poisoned with carbon tetrachloride excrete all the drug in the urine.

In connection with the use of analeptics, it may be noted that Cardiazol is rapidly absorbed from the buccal mucous membrane and from the gastrointestinal tract.<sup>12</sup>

The chemical similarity of Coramine and nicotinic acid has suggested the possible use of the former in pellagra. Spies and his associates<sup>13, 14</sup> used this substance successfully. Investigators<sup>15</sup> at Duke University have recently made a careful quantitative study of the use of this analeptic in experimental canine black tongue, an analogue of human pellagra. They showed that Coramine was able to cure black tongue in dogs, but that 30 to 75 mg per kilogram of body weight was required, as compared with 5 mg per kilogram of nicotinic acid. This would correspond in patients with pellagra to a dose of 3 to 5 gm per day.

In connection with the pharmacology of vitamins, it is to be noted that various studies of the effects of drugs on vitamin efficiency have begun to appear. Of considerable practical value is the observation of Samuels and his co-workers<sup>16</sup> that the administration of salicylates causes an increased excretion of ascorbic acid which is not due to a simple washing out. Cinchophen had a similar but slower and lesser influence. In continued dosage in rats a level of excretion was reached at which ascorbic acid balance could be maintained. The primary loss from the simultaneous administration of these anti-rheumatic drugs may be of some importance in their therapeutic use. It raises the question as to whether increased capillary permeability due to negative ascorbic acid balance could be a factor in the pathogenesis of certain rheumatic manifestations and complications, such as erythema nodosum and subacute bacterial endocarditis.

Most of this review having been devoted to analeptics, it seems appropriate to call attention to the work on morphine during the last ten or fifteen years, which has recently crystallized so

that some of the so-called "idiosyncrasies" to this drug can now be explained pharmacologically. It has become apparent that in addition to causing cortical depression morphine is a stimulant drug, and that most of the untoward reactions commonly seen in human beings can be explained on the basis of its parasympathomimetic action. Slaughter and Gross,<sup>17</sup> pupils of the late O. H. Plant, rightly point out that he<sup>18</sup> was the first to prove that the constipating action of morphine is due to the increase in tonus of the bowel produced by it. Plant also noted that denervation of the intestine increases the intensity of this action. In general, it is significant that drugs acting like neurohumoral agents produce especially violent effects on denervated organs. In Slaughter and Gross's experiments, the intestinal loops, blood pressure and toxic effects were studied as they were affected by combinations of various doses of morphine and physostigmine. A definite potentiation of the parasympathomimetic action of morphine by physostigmine was demonstrated, similar to that seen when the latter is given with acetylcholine. Since acetylcholine has been shown to be the humoral transmitter of sympathetic nerve endings in the adrenal medulla, it may be that the cholinergic action of morphine here demonstrated explains the morphine hyperglycemia described by Bodo.<sup>19</sup> The increase in toxicity when these two drugs are given together suggests a practical warning against the use of morphine in patients taking prostigmine or eserine regularly. In a further study<sup>20</sup> the effects on pain relief were studied. In this case, too, eserine potentiated and atropine antagonized the action of morphine. Morphine reacts with brain cholinesterase in vitro and lowers the serum content of this enzyme in vivo, it is potentiated by the eserine group of drugs and antagonized by atropine. It therefore fulfills the definition of a cholinergic drug, and when it is so classified the various undesirable side actions of the drug are easily explained.

In recent years, the clinical use of codeine, both alone and with drugs of the antipyretic group, has increased by leaps and bounds. Especially timely is the study<sup>21</sup> of codeine addiction carried out at the United States Public Health Service Hospital in Lexington, Kentucky, which is devoted to the study and treatment of drug addicts. A review of the literature reveals reports of 25 definite and 74 presumptive cases of addiction to this drug. In studying addiction possibilities, it was first determined that codeine could be given to morphine addicts to support physical dependence if administered in five times the dose

of morphine. However, the substitution was not complete but provided a step down in the abstinence symptoms. Similar quantitative differences are noted when the effects of codeine are studied by electroencephalographic methods, though the qualitative effects of morphine and those of codeine are similar. Codeine does not give the addict the "psychic lift." Care must be used to prescribe a habit forming drug in minimal doses for the effect desired. In the Lexington study, the effect on the cough of tuberculous patients was made the subject of carefully controlled experiments. The investigators found that 5 mg. of codeine produced relief for about three hours and 10 mg. for four hours, these doses roughly corresponded to 3 and 5 mg. of morphine, respectively. Further experiments indicate that increasing dosage provides progressively smaller increases in the duration of relief from cough. This work suggests that the dosage of codeine in cough mixtures tends to be too high, and that it is more efficient and better therapy to give smaller doses more frequently.

This review cannot be considered complete without calling attention to two very important papers<sup>21,22</sup> on sulfonamide compounds. Two excellent groups of investigators have carefully studied the toxicity, effectiveness, absorption, excretion and pharmacological action of this group of drugs. These reports may be considered authoritative and should be read by all clinicians using the drugs. Both groups emphasize the fact that sulfapyridine is definitely more toxic and more variable in its absorption than is sulfanilamide.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 26321

#### PRESENTATION OF CASE\*

A three-month-old male infant entered the hospital with a history of almost daily vomiting since the age of two days. Numerous formulas were unsuccessfully tried, and for the two weeks prior to entry, milk had been stopped and the infant fed on a mixture of barley water and carrot juice. Throughout the morning and afternoon of the day of entry the patient seemed as usual. Suddenly, in the early evening, he uttered a strange cry, developed a glassy look in his eyes, and cried as if in intense pain, thereafter he became limp. A physician was summoned, who rushed the baby to the hospital. The infant had always vomited large amounts of mucus, frequently projectively.

Physical examination showed an emaciated and moribund infant who breathed only occasionally and whose heart rate could be counted at 30 per minute. He was limp and lifeless in appearance, dirty gray in color, and appeared to be in acute peripheral circulatory collapse. The state of hydration was fairly good. The pharynx was moderately inflamed. No definite abnormality of the lungs could be made out by percussion and auscultation. The abdomen was full and soft, with no patterning, no masses or organs were palpated. All reflexes were absent. The hands and feet were cyanotic and cold.

The temperature was 98°F.

A specimen of urine was not obtained. Examination of the blood showed a red-cell count of 4,500,000 with a hemoglobin of 85 per cent, and a white-cell count of 20,000. The spinal fluid was normal. A blood Hinton test was negative. Throat culture showed no significant organisms.

The most prominent features on entry were the apnea and the signs of severe circulatory collapse. Artificial resuscitation, Coramine, oxygen and heat were used, followed by the intravenous administration of 10 per cent glucose and the subcutaneous administration of normal saline, with slight improvement in the child's general condition. Fluoroscopy showed a mottled density in

the right lower-lung field, and on this basis the administration of sulfapyridine was instituted. Improvement, however, was slight and temporary, and the infant's respirations ceased approximately five hours after entry.

#### DIFFERENTIAL DIAGNOSIS

**DR. HAROLD L. HIGGINS:** This child's past history deals mainly with vomiting and failure to utilize food properly. When we have vomiting, it is quite important to establish the cause. We have very few data here but what we do have bring out the facts that he vomited large amounts of mucus, frequently projectively, that the vomiting started at the age of two days and that he seemingly did not gain in weight. The large amount of mucus doubtless came from the stomach. When there is a large amount in the stomach, gastric digestion is not proceeding normally. I do not believe the child had pyloric stenosis, because the vomiting started early and he only vomited projectively on occasions. It seems to me there was some definite interference with the secretion of the gastric juice. There was also poor nutrition. The vomiting and the failure to handle food were so serious that milk was discontinued and only barley water and carrot juice were given for two weeks. Assuming the barley water was 3 per cent, it would contain about 3 cal per ounce, and the carrot juice would have no more, I doubt if he ingested over 25 ounces a day, which would make a total of 75 cal. If he had been on that feeding for two weeks, he must have lost a large amount of weight. He really was approaching a state of marasmus, as one gathers later from the statement that he was an emaciated infant, and perhaps he was on the verge of inanition and almost ready to die from starvation. It is hard to be certain from the available data as to whether it was as serious as that or not. Inanition cases seldom die suddenly. The inanition played a role, an important contributing role, but the fundamental cause was something else.

The sudden episode was accompanied by pain and almost immediate collapse, and the report is that the heart rate was 30. One cannot help thinking of heart block, and the main cause of heart block in children is diphtheria. The report states that the throat culture showed no significant organisms, but that does not rule out diphtheritic myocarditis with heart block. The acute diphtheria probably would have dated back two or three weeks, the actual acute inflammation in the throat could have disappeared in that time, and the culture as taken could have come back negative. One would have made the diagnosis of

\*This case is presented through the courtesy of the Children's Hospital Boston.

diphtheritic myocarditis much more readily twenty years ago than at the present. One sees very little diphtheria nowadays, but still one must be distinctly on the watch for it. A child of three months is susceptible to diphtheria.

Heart block and collapse may also come from other infections. Syphilis is quite well ruled out here, since the Hinton test was negative. Pneumonia apparently did not enter the picture, any very sick child on the slightest provocation is given sulfapyridine nowadays in hopes that it may supply a magic recovery, I am inclined to discount the pulmonary aspects in this case, particularly as nothing was found on physical examination of the lungs.

Usually in children one does not get such a low heart rate as 30 with a primary circulatory collapse. I cannot help thinking that the heart block occurred before the circulatory collapse. It is well, however, to consider the main causes of acute circulatory collapse, and one of them is damage to the medullary centers, that is, a disease of the brain. Against that is the fact that the temperature was normal, in other words the heat center was not affected. The spinal fluid was normal, and I do not see how we can accept a primary medullary condition. There was no indication of an embolus to the brain, the pain would not be so striking. A reflex collapse might come from irritation in certain parts of the body, perhaps that due to an acute pancreatitis. The fact that the patient received carrot juice raises the question as to whether the doctor in this case thought that the child had vitamin A deficiency. Acute pancreatitis is likely to lead to marked circulatory collapse. I recall one of our cases that had pain. He went into coma. We treated it as a case of diabetic coma because there was sugar in the urine, but later we found an acute pancreatitis. However, I do not believe that the condition here is abdominal. The abdomen was soft rather than tense, although in coma it might have become soft. Certainly there were no signs of peritoneal exudate or rupture of a viscus. The other main cause of collapse is hemorrhage. The blood count was normal, and there were no signs of the passing of blood either by mouth or by rectum, nor was there any purpura.

I think we have to place the main burden on the heart. There was a heart block. If this were an adult one would not hesitate to say this was a typical finding of coronary thrombosis, but in children coronary heart disease is quite rare. The rise in the white-cell count might fit in with cor-

onary disease, as does the block. It looks as if he had had an acute coronary occlusion. This acute cardiac episode is hardly likely to appear out of a clear sky, it must have had a basis. The child was not right at the age of two days, when he vomited. He never was right. One cannot help believing that the faulty digestion may have been due to difficulty in circulation. I think this child probably had a congenital malformation of the heart, which resulted in poor circulation. I should not be surprised if this congenital malformation involved the coronary arteries. I do not believe that the child's heart was markedly enlarged or showed any striking murmurs. If there had been murmurs, the doctor who had seen him—I judge there were doctors who had seen him from the fact that he had been in nutritional difficulty—would have told the mother that the child had heart disease, and the mother would have come to the hospital with that story and the approach to the case would have been somewhat different. Thus, I shall make a diagnosis of congenital malformation of the heart, probably with abnormalities of the coronary vessels. There were coronary occlusion and heart block. There were also malnutrition and marasmus. One must still consider the possibility of diphtheritic myocarditis.

Dr. TRACY B. MALLORY. Would anyone like to ask questions or suggest alternative diagnoses?

Dr. EDWARD F. BLAND. Ordinarily when you see heart block in a child you begin to think in terms of septal defect and certainly when you find something in the lungs that suggests consolidation you wonder if there has not been an infection of the lungs. There must be something superimposed on the abnormality. What did you think about the lungs?

Dr. HIGGINS. On physical examination the lungs were normal. The question of abnormality of the lung depended on what was seen on fluoroscopy. I should not be surprised if there was an early pneumonia, but the normal temperature is somewhat against it. It might have had something to do with the heart failure, but I am rather inclined to discount the fluoroscopic findings. The story is that of a sudden episode which affected the conduction fibers so as to cause heart block.

Dr. MALLORY. I have an unusual surprise for you today. We occasionally have visiting clinicians to discuss the clinical story, but ordinarily you have to bear with me, week after week, for the pathology. Today we have a visiting pathologist and Dr. Farber will tell you what was found in this patient.



## CLINICAL DIAGNOSES

Chronic nutritional disturbance  
Interstitial pneumonia

## DR HIGGINS'S DIAGNOSES

Marasmus  
Congenital malformation of heart.  
Heart block  
Diphtheritic myocarditis?

## ANATOMICAL DIAGNOSES

Congenital hypertrophic pyloric stenosis  
Malrotation of intestines, congenital  
Acute interstitial pneumonia  
Chronic nutritional disturbance

## PATHOLOGICAL DISCUSSION

DR SIDNEY FARBER\* The patient was seen by the house officers and the resident staff for a period of five hours. When the patient was examined on entry, the diagnoses were acute circulatory collapse, chronic nutritional disturbance, overwhelming sepsis and a question of pneumonia. Five hours later the diagnoses at death were chronic nutritional disturbance and pneumonia. I suppose that they decided that the pneumonia was present mainly on the basis of the appearance of the child and the evidence obtained by fluoroscopy. We unfortunately have no x-ray films.

At autopsy the skin was rather dry, and there was very little subcutaneous fat. The picture was one of marked malnutrition. The intestines were considerably distended. There was a small tumor mass at the pyloric end of the stomach. This mass was firm, almost cartilaginous in consistence. A small lumen was present, and fluid could pass through this lumen. We put this down as a moderate degree of pyloric stenosis of the congenital hypertrophic type. On microscopic examination through this area there was found a considerable increase in the thickness of the circular layer of musculature, a finding rather typical of hypertrophic pyloric stenosis.

In addition, there was another congenital abnormality. The cecum and ascending colon were not attached normally, and because of the very large mesocolon, these portions of the bowel were permitted to float over toward the left side of the body and rest on the duodenum. So in addition to the obstruction caused by a moderate degree of pyloric stenosis there was further obstruction caused by malrotation of the large bowel and partial intermittent duodenal obstruction. The his-

tory as presented is not particularly characteristic of either of these conditions.

The question does arise in regard to congenital pyloric stenosis. Is the condition an organic one or is it merely a functional abnormality of the lower end of the stomach? As you know, in the Swedish literature the claim is still made that operation is unnecessary for the correction of this anomaly, and in a number of American clinics medical treatment alone is used. We believe that this is a true organic lesion. Evidence to support this point of view was obtained for the first time when a patient of the late Dr. John L. Morse died six and a half months after a successful gastroenterostomy, to sidetrack the pyloric tumor, had been performed by Dr. Fred T. Murphy.\* Pathological studies by Dr. S. Burt Wolbach showed that the tumor was still present. Since that time this finding has been confirmed on many occasions. The first account of pyloric stenosis was published by Dr. Hezekiah Beardsley, of New Haven, in 1886. There is a distinct New England flavor to the subject of hypertrophic pyloric stenosis.

The other findings at autopsy were related to the diffuse interstitial pneumonia. The causative organism was not obtained in culture. This type of acute interstitial pneumonia is the commonest form of pneumonia found in infants and children. It is characterized by large-mono-nuclear and lymphocytic infiltration, and less commonly by polymorphonuclear infiltration of the alveolar walls and peribronchial regions. Involvement of the alveolar spaces is a later stage in the disease process. This type of pneumonia is presumably caused by a filterable virus, but this has not been proved. In most cases, within twenty-four to forty-eight hours after the onset of the interstitial pneumonia, the picture is complicated by invasion of the lung by a hemolytic streptococcus, and that organism is most frequently obtained on bacteriological examination of the lung. We found no evidence of congenital malformation of the heart or of disease of the myocardium. Our microscopic studies of the heart, however, were not of such nature as to exclude the presence of heart block.

DR HIGGINS The interstitial pneumonia as described by Dr. Farber is the condition frequently spoken of as "virus pneumonia." In this case bacterial invasion had not taken place. The virus infection seems to have been the straw which broke the camel's back, that is, it led to heart block and circulatory collapse.

\*Assistant professor of pathology Harvard Medical School pathologist Children's Hospital Boston

\*Morse J. L. and Murphy F. T. A case of infantile pyloric stenosis with autopsy six and one half months after successful gastro-enterostomy. *Boston M. & S. J.* 158:480-483 1908

## CASE 26322

## PRESENTATION OF CASE

A fifty-one year-old widow was admitted to the hospital complaining of jaundice of a few weeks duration

The patient consulted an outside physician ten months before admission because of low back pain, lack of energy, numbness and tingling in the fingers. These symptoms had followed what was described as two separate, prolonged bouts of acute alcoholism, each of which required hospitalization. The physician found that she was markedly obese, weighing 187 pounds. The blood pressure was 140 systolic, 98 diastolic. The liver and spleen were not palpable. The vibration sense appeared to be normal in the fingers, it was absent over the outer malleolus of the right lower leg, but was present on the left. The Romberg test was slightly positive. The blood and urine examinations were essentially negative. She was placed on a reduction diet, consisting of a low-fat high protein regimen supplemented with vitamin A, B and D capsules and Betaxin (5 mg) daily.

She was well until seven months before admission when she was again seen by her physician because of what was diagnosed as a virus pneumonia. She recovered uneventfully in two weeks and was apparently well until five months before admission, when her husband died. Following this she began taking as many as six to eight drinks of whiskey a day, each day's quota being augmented by a few small ones. She insisted that her diet had been adequate until at least two weeks before admission, but since that time had consisted of liquids only, because of anorexia and a difficulty in swallowing. For a few weeks before entry she had become increasingly jaundiced and she had noticed an unsteadiness in walking for a week or more. Her story was vague, and no other symptoms were elicited.

The family, marital and past histories were non-contributory.

Physical examination revealed a slightly jaundiced obese woman whose scleras were markedly icteric, but who appeared in no acute distress. The breath had a mousy odor, suggesting the presence of acetone. Examination of the lungs revealed a few rales at the left base posteriorly. The heart was normal, and the blood pressure 140 systolic, 100 diastolic. The liver was palpable about five fingerbreadths below the costal margin and was non-tender. The tip of the spleen was palpated. There was shifting abdominal dullness, but no fluid wave could be elicited because of the thick

panniculus. The deep reflexes of both upper extremities were diminished, and the patella and ankle jerks were absent. Vibration sense was poor in the fingers and absent over the malleoli of the lower extremities. There was a definitely ataxic gait. The remainder of the physical and neurologic examinations was negative.

The temperature was 101°F., the pulse 120, and the respirations 22.

Examination of the blood showed a red-cell count of 2,600,000 with 8.8 gm hemoglobin (photoelectric-cell technic), and a white-cell count of 28,000 with 81 per cent polymorphonuclears. The blood smear showed a moderate achromia, with some variation in size; the platelets were normal. The hematocrit was 20 per cent. The serum van den Bergh was 16.8 mg of bilirubin per 100 cc., with a biphasic reaction. The nonprotein nitrogen, carbon-dioxide combining power and serum protein were normal. The blood Hinton test was unsatisfactory. Examination of the urine showed a ++ test for albumin, an olive green test for sugar, and a ++ to ++++ foam test for bile, the sediment was essentially negative. The blood sugar was 186 mg per 100 cc.

The patient ran a slowly progressive downhill course. The temperature remained elevated and had an average daily range from 99 to 102°F.

She was given a high-carbohydrate, low fat, 70-gm protein diet, with barley candy at the bedside. Daily intravenous injections of glucose were administered, with small amounts of insulin to cover that excreted. A repeat blood sugar determination done eight days after admission gave a low normal value. Thiamin chloride intravenously, nicotinic acid by mouth, liver extract parenterally and periodic blood transfusions were also administered. With the latter the red-cell count rose to 3,800,000 with a hemoglobin level of 75 per cent. The white-cell count remained elevated at 23,000 with 83 per cent polymorphonuclears.

Throughout her illness she complained of pruritus. On entry she was somewhat confused and irrational. This progressed in a few days to the point where she required restraint, special nursing care and the frequent use of paraldehyde for sedation. She seemed to drift "in and out of confusion" and at night was frequently hallucinated. After about ten days, however, these symptoms disappeared and she became rational.

The jaundice steadily increased. She developed a moderate cough with rhonchi in both chests on the fifteenth day, but these symptoms were not serious or progressive. She began to develop peripheral edema, and there was no diuresis in

## CLINICAL DIAGNOSES

Chronic nutritional disturbance  
Interstitial pneumonia

## DR HIGGINS'S DIAGNOSES

Marasmus  
Congenital malformation of heart.  
Heart block  
Diphtheritic myocarditis?

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and a considerable degree of areflexia and disturbance of the vibration sense. The areflexia and disturbance of vibration sense I should assume were due to avitaminosis, and probably not connected with the liver disease. As to the lesions that might produce such a picture, the first thought, particularly in view of the very strong alcoholic history, is that of cirrhosis of the liver of the alcoholic type. There is one finding that is very unusual for that condition—the leukocytosis. In alcoholic cirrhosis the leukocyte count is usually low, and very seldom over 15,000. This makes one wonder whether we are dealing with some one of the other causes of painless progressive jaundice, such as carcinoma of the head of the pancreas or bile ducts or possibly intrahepatic primary carcinoma, such as sometimes occurs on top of alcoholic cirrhosis. I see no way that such a condition could be definitely diagnosed from the evidence at hand. I do not believe that she had biliary obstruction because of the presumable absence of clay-colored stools. I think it is quite possible that she did have two types of jaundice, one due to liver-cell destruction with the accumulation of bilirubin in the blood stream, and the other due to intrahepatic obstruction of the bile ducts as the result of long-standing liver disease. One also has to think of the possibility of silent stone, but that would seem an extremely remote possibility in this case. We are given no x-ray report, so I assume that no films were taken.

The most likely diagnosis is that of alcoholic cirrhosis in which there was a two-fold process, one a long-standing disease with cirrhotic changes and the other a recent event with extensive destruction of the liver cells, a condition which would account for the progressive jaundice, essentially like that of acute yellow atrophy, and possibly for the leukocytosis, which is unusual in the chronic alcoholic cirrhosis.

#### CLINICAL DIAGNOSES

Cirrhosis of liver, with acute liver failure.  
(Cholemia.)

#### DR. TOWNSEND'S DIAGNOSES

Acute and chronic alcoholic cirrhosis of the liver  
Avitaminosis.

#### ANATOMICAL DIAGNOSES

Alcoholic cirrhosis of the liver, slight chronic  
Acute hepatitis  
Icterus.  
Anasarca  
Bile nephrosis.  
Splenomegaly, slight.  
Esophageal varices.

DR. MALLORY: The liver was greatly enlarged, weighing 2500 gm., and perfectly smooth, a definite increase in consistence was apparent, not so much by palpation as when one made an attempt to cut it. The cut surface was predominantly pale yellow, due to very large amounts of fat, but a faint greenish tinge was apparent in some areas, thus indicating bile stasis. Microscopically there was extensive acute destruction of the liver cells, which I think we can assume occurred in the final episode. There was also slight but definite cirrhosis, which can probably be traced back to the previous periods of alcoholic indiscretion. It is often difficult in these cases to get an accurate story regarding the duration and severity of the alcoholism. In this case it could not have been very long because the cirrhosis was still of minor extent. There were a few demonstrable esophageal varices. The spleen was not markedly enlarged, weighing 300 gm. At that figure I should be skeptical as to whether it was palpated. Spleens are usually not palpable until they weigh nearly 400 gm. There was quite a generalized anasarca, and I imagine that if the serum protein levels had been determined they would have been low, probably with a reversal of the albumin-globulin ratio. Almost certainly that rather than the slight portal obstruction was the cause of the edema.

DR. JOHN D. STEWART: What about the kidneys?

DR. MALLORY: They were swollen and obviously bile stained in gross, and microscopically they showed a moderate grade of bile nephrosis.

DR. TOWNSEND: Was there any examination of nervous tissue?

DR. MALLORY: Some nerves were sectioned, but to date I have nothing but sections stained with hematoxylin and eosin, a stain which is useless in determining whether there is slight nerve degeneration.

# The New England Journal of Medicine

Formerly the  
Boston Medical and Surgical Journal

Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND  
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE  
ON PUBLICATIONS

Official Organ of

THE MASSACHUSETTS MEDICAL SOCIETY  
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United States Canada \$7.82 Boston funds (including war-exchange tax)  
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MATERIAL for early publication should be received not later than noon  
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Medicine* 8 Fenway Boston Massachusetts

## MEDICAL PREPAREDNESS THE GENERAL PROBLEM

MEDICAL preparedness is a much bigger problem than that concerned with provisions for the care of those who are wounded in action or become sick while enlisted. An adequate discussion of its many ramifications and implications would fill a book with many hundreds of pages, but it is of such importance to the safety and integrity of this country and of such vital interest to the medical profession that during the next few weeks some of the salient points will be discussed editorially. In the present editorial, the major topics of medical preparedness will be outlined.

The first, and probably the most important, of the various aspects is the health of the nation. As Surgeon General Thomas Parran\* has so ably

Parran T. Health and medical preparedness J A M A 115:49-51  
1940

pointed out, aggressive national strength—and it must be aggressive to be effective—depends on the provision not only of armament, munitions, supplies and food but also of man power, and the last is governed by physical fitness, freedom from preventable disease, and morale or mental stamina, all of which are responsibilities, directly or indirectly, of the medical profession and public health agencies.

The second point concerns the gathering of accurate information relative to the professional and technical personnel that is available for medical or public-health service, regardless of type. The proper listing of such facts is a necessity not only for mobilization but also for the provision of proper medical care for those who remain at home.

The third topic—one that is closely tied up with, if not a part of, the first—has to do with industrial workers. An unexcelled efficiency of machines is but of little advantage in times of war if it is hampered by a physical breakdown of those who man them, as a result of new industrial hazards and to the exaggeration of familiar ones, both of which are bound to accompany vast industrial expansion. Every conceivable effort must be made to protect the health of the worker and his family, in other words, the accepted ideas relative to the practice of industrial medicine must be rigidly followed.

The fourth consideration involves plans for total war: the organization of military divisions and hospitals, the training of technical personnel, the standardization of medical and surgical procedures, and the conveyance of this knowledge to regular and prospective medical officers, and the provision of adequate amounts of surgical instruments and of those drugs and biological products that are essential for proper medical care.

The whole problem is vast, in fact seems immeasurable, however, with the aid of governmental agencies, public-health departments of states and cities, the National Research Council, national voluntary organizations interested in health and disease, and the medical and related professions, it can be accomplished. Some sort of a coordinating agency is obviously necessary. Surgeon

General Parran has suggested that a co-ordinator of medical and health preparedness be appointed under the National Defense Council." The responsibilities seem to be too varied and too great to be shouldered by any one individual, and a full-time board composed of four or five men, each of whom is an expert in one or another of the aspects of medical preparedness, would appear to offer the logical solution. In any event, the success of the plan—like that of any huge undertaking—demands careful planning, intelligent co-operation and unstinted sacrifice.

### QUARTERLY JOURNAL OF STUDIES ON ALCOHOL

Within the past five years the attention of scientists has been redirected toward the problem of alcoholism and related conditions. It is pleasing to note that the hysterical interest shown during the era of prohibition has waned and has been replaced by scholarly studies representing all interests. In order to foster an impartial point of view, the Research Council on Problems of Alcohol, an affiliate of the American Association for the Advancement of Science, was organized—a step which was commented on editorially in the February 15 issue of the *Journal*.

Recently the first number of the first volume of the *Quarterly Journal of Studies on Alcohol* made its appearance. The Research Council on Problems of Alcohol has chosen the new journal as its official organ, and the editorial board is composed of members of the scientific committee of that organization. Massachusetts is represented by Drs. Thorne M. Carpenter, Merrill Moore and Abraham Myerson. The journal is published in New Haven and is edited by Dr. Howard W. Haggard, of Yale University, and Dr. Nathan Rakieten.

Librarians have been known to state that there are too many medical journals and that several could be eliminated without loss. However, this newest one will serve a distinctly useful function in providing a medium for the increasingly large

number of scientific studies that are being carried out in the United States for the purpose of ascertaining the nature and needs of alcoholic individuals. Not all the articles that appear in the first issue of this journal represent definitive or therapeutic studies. The forensic viewpoint is presented through a section entitled "Medicolegal Reviews," and in this maiden number it is concerned with "Chemical Tests to the Proof of Intoxication under Workmen's Compensation Statutes."

Of nine original articles two are psychiatric in nature, three are biochemical, two are pathological and two are statistical. All this demonstrates a praiseworthy effort to cover various and different phases of alcoholism. The format is superior and dignified, well becoming the serious attitude toward the problem of the persons whose work is represented. One article deserves special mention. Dr. Nolan D. C. Lewis, writing on "Personality Factors in Alcoholic Addiction," expresses the attitude of all unbiased students of alcoholism, namely, that the condition represents a neurosis, a psychiatric aberration, and that it must be approached with this in mind before progress in treatment can be expected.

With the threatened suspension of publication by the *British Journal of Inebriety* and several Continental journals covering essentially the same subject this new journal may become the only one in English devoted solely to the collection and presentation of information concerning alcohol and alcoholism.

It cannot be said that alcoholism is decreasing. The most hopeful promise that it will decrease is the fact that it is now coming to be recognized as a medical and psychiatric problem and is being studied and treated accordingly. Evidence that the heavy artillery of modern scientific medicine is being brought to bear on alcoholism can encourage the belief that it may in a reasonably short time take its place among the public-health problems that are definitely under control. The *Quarterly Journal of Studies on Alcohol* will render service to this end. May it have health and a long life!

## MEDICAL EPONYM

### COLLES'S LAW

The following excerpt is seldom quoted exactly as Abraham Colles (1773-1843) gave it in his *Practical Observations on the Venereal Disease, and on the Use of Mercury* (London: Sherwood, Gilbert and Piper, 304, 1837)

One fact well deserving our attention is this that a child born of a mother who is without any obvious venereal symptoms, and which, without being exposed to any infection subsequent to its birth, shows this disease when a few weeks old, this child will infect the most healthy nurse, whether she suckle it, or merely handle and dress it, and yet this child is never known to infect its own mother, even though she suckle it while it has venereal ulcers of the lips and tongue

R W B

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

RAYMOND S. TITUS, M.D., *Secretary*  
330 Dartmouth Street  
Boston

### PNEUMONIA IN PREGNANCY, EMPYEMA

Mrs. G. R., a twenty-four-year-old para II, in the fifth month of pregnancy, telephoned on May 26, 1925, that she had a cold of several days' duration. The night before she had had a chill, and shortly afterward severe pain over the right apex posteriorly when breathing or coughing. An internist was called in consultation.

The family history was negative except there was said to be some tuberculosis on the maternal side. None of the immediate family had ever had any lung symptoms, but the patient was said to have always been "weak" and to have had three or four pulmonary hemorrhages. There was no history of chronic cough or loss of weight. The past history included the usual children's diseases. A tonsillectomy had been performed in 1918. Catamenia began at twelve, were regular with a twenty-eight-day cycle and lasted five days without pain. The last period began on December 20, 1924, making the expected date of delivery September 27. The previous pregnancy had been uneventful and had terminated in a simple forceps delivery on November 19, 1923. The present pregnancy had been normal.

Physical examination revealed a temperature of

100.4°F and a pulse of 100. The throat was normal, there were no enlarged lymph nodes. The heart was rapid but regular, with a soft, systolic murmur at the apex. The lungs showed definite dullness in the right apex, with a few rales which were heard after forced breathing and after coughing, there was no bronchial breathing. The abdomen was negative except for a tumor consistent in size with a five-month pregnancy. There was no edema. The consultant thought that the patient had pneumonia, and she was advised to enter the hospital. This was effected several hours later.

On admission the temperature was 102°F, the pulse 120, and the respirations 35 to 40. There were bronchial breathing and signs of consolidation at the right apex. Sputum examination showed no acid-fast bacilli. On May 27 the white-cell count was 6400. The patient complained of abdominal pain, although the obstetrician did not believe that the uterus was contracting. About half an hour after he saw her she had some bloody discharge, and within an hour she was in labor. Under nitrous oxide and oxygen anesthesia she eventually delivered herself of a five-month still born fetus without any difficulty.

On May 29 it was thought that the pneumonia had possibly extended into the left lung. An x-ray film taken on June 1 showed questionable fluid at the base of the right lung, but no evidence of tuberculosis. On June 4 the temperature was still around 99°F, there were additional signs of fluid at the right base. On June 7 the patient complained of pain over the right back and right shoulder, the signs of fluid were more marked. A second x-ray film taken on June 9 showed obvious fluid at the right base. The chest was tapped, and turbid fluid containing many pneumococci obtained. A second tap was done on June 10, again with the recovery of cloudy fluid. A surgical consultation was held, but postponement of operation was advised. During this time the temperature ranged from 101 to 102°F. On June 13 the chest was again tapped, and moderately thick pus was obtained. An operation was performed, and a large, apparently definitely walled off, empyema cavity was found. Following operation the temperature rose to 102.6°F on June 17, and to 101.6 on June 23. There was a dull area at the right of the sternum, which by x-ray proved to be a patch of unresolved pneumonia. On June 29 the temperature rose to 103.2°F. A consultation was held, but the consultant believed that there was no indication for operative interference. The following day the temperature was normal. On

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

July 3 the temperature rose following the changing of tubes and the patient developed a severe cough, with the raising of thick, yellow, foul sputum. Moderate amounts of greenish sputum, not definitely foul, persisted for a few days. By July 10 all that remained was an irritating, nonproductive cough. On July 14 a deep abscess in the right thigh, which had resulted from an injection of ergot, was evacuated, and on July 25 the patient was discharged home. The drain was removed on August 8.

At an office examination on November 16 no abnormalities were noted, the empyema wound had satisfactorily healed.

**Comment** It is really not quite fair to infer that pregnancy had any great influence on this case of pneumonia, with its serious complications. The patient was treated ideally from the start. The pneumonia developed very quickly following a cold. The patient was seen by a medical consultant at the very beginning of the illness, and hospitalized as soon as possible. The labor was very simple, and was accompanied by no real distress and no unusual loss of blood. It is not too optimistic to infer that chemotherapy might well have prevented the unresolved pneumonia and the development of the empyema. The patient subsequently had two uneventful pregnancies.

## DEATHS

**HALSALL**—**MARY ELIZABETH HALSALL, M.D.** of Winthrop, died August 1. She was in her seventy-sixth year.

Born in East Boston she received her medical degree from Tufts College Medical School in 1903. She practiced in East Boston the greater part of her life and had been associated with the New England Hospital for Women and Children for many years.

Dr. Halsall was a retired member of the Massachusetts Medical Society, the American Medical Association and the New England Women's Medical Society.

Her widow, a daughter, a son and a grandson survive her.

**LATHAM**—**BENONI MOWRY LATHAM, M.D.**, of Mansfield, Massachusetts, died July 24. He was in his sixty-eighth year.

Born in Smithfield, Rhode Island, he received his medical degree from Harvard Medical School in 1900. He served with the medical corps during the World War.

Dr. Latham was a member of the Massachusetts Medical Society, the American Medical Association and the Mansfield Doctors' Club.

His widow, two sons, a daughter, a brother, a sister and several grandchildren survive him.

## MISCELLANY

### ENROLLMENT OF VOLUNTARY BLOOD DONORS

The American Red Cross, acting at the request of the Surgeon General of the U. S. Army, recently announced experimental plans for the promotion of a nationwide

corps of volunteer blood donors which would become part of the national defense program, when and if needed.

Chairman Norman H. Davis, in announcing the proposed program, declared the plan would be to make available blood plasma to the U. S. Army Medical Corps in the event of emergency. For the past four years he said twelve Red Cross chapters have been furnishing whole blood from volunteers to hospitals for civilian use. The new program will be patterned along similar lines using plasma instead of whole blood, it was explained. A preliminary study involving 1300 Red Cross volunteers in four cities throughout the country will be conducted under the direction of a special committee appointed by the National Research Council, Chairman Davis said.

Dr. William DeKlene, national medical adviser of the Red Cross, said that the proposed plan for collecting blood was patterned after the blood-bank idea except that plasma will be used instead of whole blood. Plasma, he explained, is as satisfactory as whole blood in the treatment of hemorrhage and shock. "Plasma," Dr. DeKlene pointed out, "has many advantages over whole blood. The latter can be kept only a few days because the red blood cells deteriorate very quickly. Plasma can be kept indefinitely does not require typing and can be moved about freely without any damage to it. It can be transported any distance and is therefore applicable in military as well as civilian practice. Preliminary studies must be made to perfect methods of collecting, storing and administering plasma under conditions comparable to war-time emergency. Blood for this initial study will be furnished by volunteers at the various hospitals where members of the Research Committee are regularly employed. The plasma collected will be stored and used as emergencies arise at these hospitals."

After these preliminary investigations have been completed, the Red Cross will work out with the medical department of the U. S. Army plans for enrolling prospective donors in cities throughout the country where collecting centers will be established. In the event of an emergency the Red Cross could start delivering plasma within ten days after enrollment is completed, Dr. DeKlene said. Blood so collected will be pooled in large sterile containers to simplify storage, in sufficient quantities to meet the emergency needs for treating the wounded.

Recruiting donors will be conducted by a special blood-transfusion committee of the local chapter which will include leading physicians. The technical phases of the project will be performed by the medical staffs of the cooperating hospitals. They will examine the prospective volunteers, make the necessary blood tests and bleed those who are found to be satisfactory.

## NOTES

Appointments to the teaching and research staff of the Harvard Medical School and Harvard School of Public Health were recently announced by the University as follows:

In the Harvard Medical School effective September 1, 1940: Walter H. Sheldon, M.D., Royal University of Lausanne, Italy, 35, now at the Free Hospital for Women, Brookline, instructor in pathology; Oscar D. Ratnoff, M.D., Columbia University, 39, now at Johns Hopkins University Hospital, Assistant Teaching Fellow in Physiology; Bernard J. Jandorf, A.M., Harvard, 40, of Brookline, teaching fellow in biological chemistry; Charles L. Sturdevant, M.D., University of Nebraska, 36, now at Children's Hospital, Boston, assistant in orthopedic surgery; Robert M. Crowder, M.D., Northwestern University, 37, of Bos-



ton, assistant in roentgenology, Walter L. Hughes, Ph.D. Massachusetts Institute of Technology '40, of Boston, research fellow in physical chemistry, and Bernard Bandler, 2nd, M.D. Columbia '38, now at Boston City Hospital, assistant in psychiatry.

In the Harvard Medical School, effective January 1, 1941 Bruce R. Merrill, M.D. Harvard '38, now at Boston Psychopathic Hospital, assistant in psychiatry.

In the Harvard School of Public Health, effective September 1, 1940 Floyd D. Hager, Ph.D. University of Illinois '26, of Brookline, instructor in applied immunology, and Ralph W. McKee, Ph.D. St. Louis University '40, of St. Louis, instructor in industrial hygiene.

The July issue of the *Archives of Pathology* is dedicated to Dr. S. Burt Wolbach, Shattuck Professor of Pathological Anatomy at the Harvard Medical School and pathologist at the Peter Bent Brigham Hospital. As is customary, all the papers have been contributed by his present and former students and associates.

## REPORTS OF MEETINGS

### SUFFOLK DISTRICT MEDICAL SOCIETY

A regular meeting of the Suffolk District Medical Society, held at the Boston Medical Library on March 27, was devoted to a discussion of "Diarrhea." Dr. Reginald Fitz presided.

The first paper, on "Acute Infectious Diarrhea," was read by Dr. Roy F. Feemster, of the Massachusetts Department of Public Health. The speaker traced the decrease in most diarrheal diseases, particularly the serious ones, since 1860 and showed its correlation with the perfection of sanitation, the pasteurization of milk, and the recognition of carriers among food handlers. Typhoid fever has diminished from 88 cases per 100,000 in 1860 to 0.2 at the present time, while paratyphoid fever, which has never caused more than two deaths per year in this state, seems to be gradually increasing. The latter is partly due to better diagnosis and more diligent search, it was added. Dysentery, which takes its toll particularly in infants and in the aged, has been changing in the type of responsible organism. Whereas the Flexner strain was the chief etiologic agent prior to 1937, this has not increased recently, while the Sonne strain has shown a remarkable rise, particularly in sporadic cases.

Diarrhea and enteritis in infants have also shown a decrease. Since these conditions are particularly prone to strike during the summer, the significant factors in the reduced incidence have been pasteurization of milk, refrigeration of milk and food, and education of the mother in regard to regulating the child and his environment. In this age group in particular, stated Dr. Feemster, certain outbreaks may be attributable to virus infection, for in maternity wards the spread may be explosive and brought about by only casual contact.

In spite of the reduction in the prevalence of the more serious varieties of intestinal diseases, diarrhea is still one of the frequent ailments seen by the physician. In most cases the duration is short and the illness mild, but we must be continually on the alert to make sure that the next case seen is not one of the more serious varieties. Typhoid fever, paratyphoid fever and dysentery are still endemic and may at any moment occur in the practice of a physician. Dr. Feemster indicated that although there is no reliable way of making an estimate, probably 10 to 25 per cent of the population have diarrhea at some time during each year, and yet only 25,000 of this hypothetical half million to a million people can have their

stools examined in a recognized laboratory with the facilities now available. In order to choose appropriate cases for bacteriological study, the following conditions are particularly applicable: blood or mucus in the stool, an unexplained fever in the presence of diarrhea, a diarrhea lasting more than forty-eight hours, cases with marked prostration, especially in infants, secondary cases, and multiple cases occurring at any time in a family, even in the absence of the above findings.

In regard to follow up, Dr. Feemster suggested observing precautions until three negative stools have been obtained. The basis for this precaution is well borne out by the statistics on the number of stools examined in cases of paratyphoid fever before they were negative. Bacilli were present in half the cases in the fifth week and 12 per cent in the ninth week, and not until the thirtieth week were only 3 per cent — the permanent carriers — positive.

"The Maintenance of Adequate Nutrition in Chronic Diarrhea" was the title of the discussion by Dr. Maunce B. Strauss of the Boston City Hospital. He stated that although purified vitamin preparations are rarely needed for the maintenance of nutrition in the normal person, deficiencies of vitamins, minerals and protein are prone to develop in chronic diarrhea. Such deficiencies may result from an inadequate intake, poor absorption or an increased need of these substances. In addition, a vicious circle may be formed in chronic diarrhea where an avitaminosis, particularly of the vitamin B complex, may cause such changes in the gastrointestinal mucosa as to prolong the diarrhea.

Vitamin K deficiency may result from a variety of disturbances of the biliary or intestinal tracts, but no symptoms occur until the prothrombin falls to 25 to 30 per cent of normal. The intravenous administration of synthetic vitamin K has shown immediate and striking results, but the substance should be administered by mouth or intramuscularly for sustained effect.

Ascorbic acid is particularly necessary as an auxiliary food factor in diarrhea, for natural food sources of vitamin C may be poorly tolerated in this condition.

Patients with pernicious anemia are prone to diarrhea, and liver extract by mouth in such people may be poorly absorbed. A case was cited where one one-hundredth as much extract parenterally proved effective where the oral route had failed. Similarly, iron absorption is diminished and the intake usually limited by the dietary restrictions.

Dr. Strauss discussed briefly the chief findings of other vitamin deficiencies which may occur during chronic diarrhea. A lack of vitamin A leads to poor dark adaptation, of riboflavin to cheilosis and fissures at the corner of the mouth. Vitamin B therapy is effective in relieving the peripheral nerve and cardiac symptoms of its deficiency, and nicotinic acid combats the glossitis and the dermatitis of the exposed or irritated parts seen in pellagra.

The optimum treatment for a patient with chronic diarrhea was summed up by Dr. Strauss. It should include an adequate intake of calories and proteins, the latter often by necessity being supplied wholly or largely by milk and eggs, and vitamins and minerals in their natural form in fruits and vegetables, when possible. Dr. Strauss suggested the daily use of 5000 units of vitamin A, 2 mg of thiamin chloride (probably), 100 mg of nicotinic acid, 7 mg of riboflavin, 100 mg of cevitamic acid, 1000 units of vitamin D, 2 to 3 gm of calcium, 30 mg of iron, 1 to 2 mg of vitamin K, and a minimum of 100 gm of protein.

The discussion was opened by Dr. Chester M. Jones of the Massachusetts General Hospital, who called attention to the striking incidence of infectious diarrhea pre-

vailing during the winter months. Unlike the results with the summer diarrheas of children, public-health measures have failed to lower the incidence of such disturbances, which frequently occur in epidemics as well as sporadically. Many such cases are undoubtedly due to outbreaks of Sonne dysentery but in addition he raised the question as to the possibility of a virus infection which might warrant careful study. The importance of such outbreaks was stressed, inasmuch as some of the more severe cases, particularly those of Sonne dysentery appear to possess all the characteristics of subacute ulcerative colitis and to be indistinguishable from this serious condition. He also mentioned the apparent increase in infectious diarrhea due to various causes such as dysentery bacilli, amebae and the like, incident to winter cruises and airplane travel to subtropical and tropical areas. An apparently innocent case of infectious diarrhea should be watched carefully if blood appears in the stools. Such can occur in cases of Sonne dysentery for example, but also may be a first warning of a serious ulcerative colitis. He stressed the importance of the maintenance of nutrition in all cases of prolonged diarrhea with particular reference to those occurring in infants and young children. Even in adults, however especially when severe diarrhea persists over a period of several days, the use of transfusions and parenteral fluids may be of importance.

Dr Charles F. McWhann, of the Children's Hospital discussed diarrhea in children and suggested that the increase, at least in institutional epidemics indicates the extreme infectiousness of the Sonne strain for even good isolation has sometimes failed to prevent cross-infection. That poor technique of bathing is at least partially responsible is evidenced by the large number of such epidemics in Massachusetts, where the incidence of flies is relatively low in treating diarrhea. It was advised that those with dysentery which is essentially a constitutional disease, can tolerate food a day or two after the acute symptoms have subsided, while those with gastroenteritis have residual intestinal irritation and should not be offered nutrition for some time.

#### HARVARD MEDICAL SOCIETY

A regular meeting of the Harvard Medical Society with Dr Elliott C. Cutler presiding was held at the Peter Bent Brigham Hospital on April 23.

The first case presented was that of a young man with a typical history of peptic ulcer which was refractive to medical care and eventually necessitated surgery. Dr Cutler described the newer type of operation which attempts to reduce more effectively the prevailing acidity by removing the folds of fundic mucosa. This leaves only a tube of stomach along with what was formerly the lesser curvature, and the secreting surface is thus markedly decreased. Dr E. S. Emery stated that the immediate results of this operation appear better than those of former methods. He also said that failure to control ulcer symptoms by a truly adequate medical regimen probably indicates either a lack of control of the acidity or a penetrating lesion. It was suggested, therefore, that such cases be chosen early for elective surgical treatment.

The medical case was that of a twenty-seven-year-old man who had had intermittent headaches for two months. One year before entry the patient had developed nasopharyngitis, and eight months later "back pain" which was treated with a low salt, low protein diet. The headaches had become more severe, and two weeks before admission there was blurring of vision followed shortly by bouts of nausea and vomiting. The family history was significant only in that the patient's mother had died of

Bright's disease at thirty-two years of age. Physical examination revealed fundic changes compatible with hypertensive encephalopathy, an enlarged heart and a blood pressure of 206 systolic, 156 diastolic. At times there were twitchings and the patient was very restless. Laboratory findings of significance were a moderate anemia, a blood-calcium of 4.9 mg per 100 cc., a nonprotein nitrogen of 115 to 135 mg. and a normal total blood protein. Dr Soma Weiss suggested the diagnosis of malignant hypertension and malignant nephrosclerosis without any evidence of preceding glomerulonephritis or pyelonephritis. The fact that the initial manifestations might be referable to the head and uremia was emphasized. Dr Weiss discussed the yellowish-brown pigmentation which often occurs in nephritis as a result of failure to excrete urochrome. A warning was issued against ill-advised brain surgery on the basis of the true papilledema and the occasional increased cerebrospinal-fluid pressure found in hypertensive encephalopathy.

The speaker of the evening was Dr W. J. Merle Scott of Rochester, New York, who discussed "Some Problems in the Proper Emptying of Hollow Viscera." He first considered the urinary bladder the emptying of which is controlled by the sacral parasympathetic efferents. It was pointed out that cord injuries or tabes dorsalis affects the parasympathetic fibers so that there is a resultant imbalance of innervation. The cystometrogram has proved indispensable to the establishment of the type of bladder difficulty both initially and during treatment. Presacral neurectomy to tabes dorsalis by removing the normal sympathetic inhibition, often improves bladder function. In the chronic cystitis found in genitourinary tuberculosis, some improvement may often result by the removal of the fibers which innervate the region of the internal sphincter and trigone.

Surgery for the benefit of faulty large-bowel function centers largely around the treatment of megacolon. A preoperative test with spinal anesthesia should be used to clinch the fact that there is truly an imbalance of innervation in favor of the sympathetic system and then some form of sympathectomy should be done. In young men on whom presacral neurectomy is performed care should be taken not to divide the fibers from the first lumbar ganglion, for this prevents ejaculation.

In regard to cardiospasm of the esophagus, Dr Scott emphasized the importance of differentiating the purely spastic type and that wherein hypertrophy is the outstanding characteristic. Spinal anesthesia with its accompanying sympathetic paralysis is also a helpful diagnostic procedure, and operation should be carried out only where sympathetic overbalance is definitely an important or the sole factor. Resection for peptic ulcer has been known to alleviate the symptoms of cardiospasm. An operation was suggested whereby the esophagus is brought down after resection and a new opening is made.

The discussion was initiated by Dr Walter B. Cannon who stated that the essential function of the extrinsic nerves to the hollow viscera is an increase of tone from parasympathetic and a decrease from sympathetic innervation. The stretch stimulus parallels the tone in general so that on gradual filling an increased tone in a sensitive organ causes the threshold stimulus to be reached earlier a fact which explains the role of the dual innervation and the imbalance that causes faulty emptying. Dr Cannon also stated that the denervated esophagus and stomach eventually develop an adequate independent tone. Conditions which may decrease the intrinsic tone and so cause poor emptying of hollow viscera include a depressed physical condition with its generalized decreased muscular tone, emotional upsets where sympathoadrenal stimula

tion reigns and persistent sympathetic overstimulation as found in Hirschsprung's and Raynaud's diseases

Dr James C White discussed cystograms and colometrograms under normal, pathologic and treated conditions, he showed the parallelism between the curves for the various conditions in the two organs. Further studies on the results of the surgical treatment of megacolon demonstrated that the haustrums remain as a result of the intrinsic plexi of Meissner and Auerbach but that the rush peristalsis is lost. An interesting observation was that presacral, lumbar or splanchnic neurectomy has no effect on the emptying of hollow viscera in normal individuals.

Dr Cutler urged that one remember that spinal anesthesia may cause a permanent rather than merely a temporary improvement in Hirschsprung's disease. A warning was also issued to the effect that intraspinal novocain may be more injurious in some patients than is commonly supposed.

Dr William C Quinby reported disappointing results in the treatment of painful urinary bladders by neurectomy, especially when the underlying disease is an interstitial cystitis.

#### WORCESTER NORTH DISTRICT MEDICAL SOCIETY

A regular quarterly meeting of the Worcester North District Medical Society was held Wednesday, July 24, at 1 00 p m, at the Henry Heywood Memorial Hospital.

After an excellent dinner, the president, Dr B P Sweeney, called the meeting to order. The records of the previous meeting were read and approved. After a discussion of the "Gentlemen's Agreement" and the blank for patients to sign, giving permission to the insurance companies to pay the physician direct, the president spoke of the meeting in Boston of the committee of the Massachusetts Medical Society and representatives of the insurance companies. He mentioned the following points in formation concerning the injuries of a patient should not be discussed over the telephone, written consent of the patient should be obtained before any information concerning the patient is given, any discussion of the patient's injuries or condition must not be discussed with the physician representing the insurance company, except in the presence of the patient.

A communication was read from the National Physicians Committee, describing the progress being made and appealing for members and for money to continue their work. Dr J J Curley moved that the society donate the sum of \$50 for this purpose. This was seconded by Dr C B Gay and voted unanimously.

The resolution of the special committee of the Committee on Public Relations of the Massachusetts Medical Society to study medical-costs insurance plans was then read.

Under reports of committees, Dr R F Bachmann reported that the Legislative Committee did not approve Senator Lodge's substitute measure for the Wagner Bill, as it was just another attempt at concentration of federal authority in Washington. It was moved that this information be sent to Senator Lodge as the feeling of this society. Dr T R Donovan then proposed an amendment to this motion, namely, that this report include the reasons of the committee for its non approval, together with an expression of appreciation of Senator Lodge's motives in making his proposal, which is such an improvement over the Wagner Bill. This amendment was passed without dissenting votes.

Dr Curley then disclosed another proposal of the federal government, whereby \$14,000 would be appropriated this year for the segregation of all new cases of rheumatic

fever with involvement of the heart at three cities in the State—Boston, Worcester and Springfield. These would be cared for by three consultants under the direction of the State Department of Public Health. He described the various conditions, regulations, board fee and so forth prescribed and requested the opinion of the society as to how he should vote at the meeting of the Committee on Public Relations. Dr F Thompson moved that the report of Dr Curley be accepted and that the society instruct him to vote against acceptance of this measure. This was passed without dissenting votes.

Dr Curley then discussed the lack of support given congressmen in Washington and recommended that the members of the society show their interest by sending telegrams. He then moved that the secretary be empowered to send a telegram to any legislator with the names of members of the Worcester North District Medical Society in favor of or opposed to any measures affecting the society or the medical profession, provided sanction has been given by the Legislative Committee. This motion was passed.

The speaker of the day, Dr Alan Moritz, professor of legal medicine at Harvard Medical School, then spoke on "Tales That Dead Men Tell." He discussed the percent age of medicolegal deaths and the percentages of accidents, suicides and homicides in this group. He showed lantern slides of interesting cases and spoke of the methods in use to determine causes of death. His material had been assembled from all parts of the world and was very interesting. The slides showed many cases of suicide and homicide, and he discussed the points that led to the final decision. He also showed several cases which were thought to be caused by trauma but were due to natural causes, and the opposite.

## NOTICES

### ANNOUNCEMENT

WALTER F LEVER, M D, announces the opening of an office at 270 Commonwealth Avenue, Boston.

### AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The following action regarding case records to be submitted by candidates taking the Group B, Part I, examination after January 1, 1942, was passed by the American Board of Obstetrics and Gynecology at its annual meeting in Atlantic City, New Jersey, on June 6, 1940: "Case records submitted by candidates must be of patients treated within four years prior to the date of the candidate's application. The number of cases taken from one's residency service should not be more than half of the total number of fifty cases required."

In response to numerous inquiries regarding special training requirements, the Board desires again to announce that there are three methods of meeting these requirements for admission to examination. First, by the residency system, second, by the partial residency and partial assistantship method, and third, entirely by the assistantship or "preceptorship" method. Details of the residency requirements are given in the booklet that is forwarded by the Board on request.

The Board will accept in lieu of the formal residency service the training acquired by a candidate serving on an assistant or dispensary staff of an obstetric and gynecologic division of a recognized hospital, under the direction of a recognized obstetrician gynecologist (preferably a diplo-

nate) The time required for this type of training must be longer than that with the formal, more intensive, residency type of training and the allowance of time depends on the duties and responsibility given the candidate. Applicants lacking all formal special training should have a minimum of five years of hospital-clinic or assistant hospital-staff appointments in the specialty under approved direction. Teaching appointments without accompanying hospital staff or clinical appointments will not satisfy the requirements. A special form amplifying the original application must be filled out to cover the details of such assistantship or preceptorship type of training. For special training the Board approves work done in institutions approved jointly by the Board and by the Council on Medical Education and Hospitals of the American Medical Association.

For further information address Dr Paul Titus, Secretary 1015 Highland Building Pittsburgh, Pennsylvania

## SOCIETY MEETINGS AND CONFERENCES

SEPTEMBER 2-6—American Congress of Physical Therapy Page 862, issue of May 16.

OCTOBER 6-11—Annual meeting of the American Academy of Ophthalmology and Otolaryngology Page 81 issue of July 11

OCTOBER 8-11—American Public Health Association Page 655 issue of April 11

DECEMBER 11, 12—Pan-American Congress of Ophthalmology Page 854, issue of May 23.

DECEMBER 14-25—1940 Graduate Fellowship of the New York Academy of Medicine. Page 934 issue of May 30

OCTOBER 21—American Board of Internal Medicine. Page 309 issue of February 29

JANUARY 4, 1941—American Board of Obstetrics and Gynecology Page 1064 issue of June 20

MARCH 8—American Board of Ophthalmology Page 201 issue of August 1

APRIL 21-25—American College of Physicians. Page 1065 issue of April 30.

## BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

*Behind the Scenes of Murder* By Joseph Catton M.D., clinical professor of medicine, Stanford University 8 cloth 355 pp. New York W W Norton & Company Inc. \$3.00

*Report on the Sex Question by the Swedish Population Commission* A publication of the Medical Aspects of Human Fertility Series issued by the National Committee on Maternal Health, Inc. Translated and edited by Virginia Clay Hamilton, M.D. 8 cloth, 182 pp with 9 tables. Baltimore Williams & Wilkins Company 1940 \$2.00.

*Clinical Practice in Infectious Diseases for Students Practitioners and Medical Officers* By E. H. R. Harries, M.D. (Lond.), M.R.C.P., D.P.H., medical superintendent North-Eastern Hospital (London County Council) and M. Mitman, M.D. (Lond.) M.R.C.P., D.P.H. D.M.R.E., medical superintendent, River Hospitals with a foreword by W. Allen Daley M.D. (Lond.) F.R.C.P., D.P.H., medical officer of health London County Council 8 cloth, 468 pp., with 31 illustrations and 28 tables. Baltimore Williams & Wilkins Company 1940 \$6.00

*Physiology of Micturition Experimental and clinical studies with suggestions as to diagnosis and treatment.* By Orthello R. Langworthy M.D., Lawrence C. Kolb M.D. and Lloyd G. Lewis, M.D. A publication of the sub-department of neurology and the James Buchanan Brady Urological Institute, Johns Hopkins University 8 cloth 232 pp with 49 illustrations. Baltimore Williams & Wilkins Company 1940 \$3.50.

*Gynecological and Obstetrical Pathology with Clinical and Endocrine Relations* By Emil Novak A.B., M.D. D.Sc. (Hon., Dublin) associate in gynecology Johns Hopkins School of Medicine, and gynecologist, Bon Secours and St. Agnes hospitals, Baltimore. 8 cloth, 496 pp., with 427 illustrations. Philadelphia W B Saunders Company 1940 \$7.50

*Atlas of Cardioradiology* By Hugo Roessler M.D., associate professor of roentgenology and cardiologist in the Department of Medicine, Temple University School of Medicine and Hospital, Philadelphia. F cloth, 124 pp., with 166 illustrations. Springfield Illinois Charles C Thomas 1940 \$8.50

*Diseases of the Digestive System A textbook for students and practitioners* By Eugene Rosenthal, M.D., lecturer in the medical faculty Royal Peter Pazmany University Budapest, Hungary, with a preface by R. J. V. Pulvercraft, M.D. F.R.C.P., reader in pathology University of London, and director of the John Burford Carlill Laboratories and curator of museum Westminster Hospital School of Medicine. 8 cloth 394 pp. with 234 illustrations including 104 in color and 16 tables. St. Louis C. V. Mosby Company 1940 \$8.50

*Rheumatic Fever Studies of the epidemiology manifestations diagnosis and treatment of the disease during the first three decades* By May G. Wilson M.D. A publication of the New York Hospital and the Department of Pediatrics, Cornell University Medical College, New York City 4 cloth 595 pp. with 47 illustrations, 76 figures, 81 tables and 31 charts. New York Commonwealth Fund 1940 \$4.50

*A Research Conference on the Cause and Prevention of Dental Caries* Chicago Illinois July 1 and 2 1938 8 cloth 178 pp with 11 figures 12 tables, 6 charts and 6 graphs. Chicago Good Teeth Council for Children Incorporated 1940

## BOOK REVIEWS

*Combined Textbook of Obstetrics and Gynaecology for Students and Medical Practitioners* Revised and rewritten by J. M. Munro Kerr LL.D., M.D., F.R.F.P.&S. (Glas.) F.R.C.O.G. Third edition. 8, cloth 1192 pp with 499 illustrations and numerous ray plates. Baltimore Williams & Wilkins Company 1939 \$12.00

The revision of this book has been performed by seven eminent British co-authors. The volume is compactly written and incorporates the present fundamental knowledge concerning obstetrics and gynecology. Modern facts of endocrinology are presented in appropriate portions of the text, but little experimental or controversial material has been admitted.

The section on obstetrics comprises almost two thirds of the volume. The section on gynecology is divided into medical and surgical considerations of this branch of medicine. The medical aspects are presented in sufficient detail while in the portion devoted to surgery the illustrations adequately present the steps in technique.

The last chapter is devoted to modern roentgenological technic in obstetrics and gynecology. It presents all the essential advances made during the past five years.

This text is an excellent standard treatise on the combined specialties of obstetrics and gynecology. It should be of great value to all English speaking students and practitioners. Its arrangement should serve as a model for any contemplated one-volume treatise on these subjects.

*Compendium of Regional Diagnosis in Lesions of the Brain and Spinal Cord. A concise introduction to the principles of localization of diseases and injuries of the nervous system.* By Robert Bing. Translated and edited by Webb Haymaker. 11th edition. 4°, cloth, 292 pp., with 125 illustrations and 7 plates. St. Louis: C. V. Mosby Company, 1940. \$5.00.

Bing's book on regional diagnosis in lesions of the brain and spinal cord has long been a standard introductory text in this country. It is now in its eleventh edition. Under new form, and by a new translator, the present volume is welcome. The book is accurately written, it can be recommended to medical students and physicians.

*Sexual Pathology. A study of derangements of the sexual instincts.* By Magnus Hirschfeld, M.D. Authorized translation by Jerome Gibbs. 8°, cloth, 368 pp. New York: Emerson Books, 1940. \$2.95.

This book is one of the standard texts on the subject, taking its place with that by Krafft-Ebing. Formerly published in three large volumes, the present issue is an abridgment, giving the essentials as depicted by Hirschfeld, formerly of the Institute of Sexual Science in Berlin. The book is well printed and can be recommended as an exposition of the subject, although few will agree with all the author's conclusions.

*Cancer with Special Reference to Cancer of the Breast.* By R. J. Behan, M.D., Dr. Med. (Berlin), F.A.C.S. 4°, cloth, 844 pp., with 168 illustrations and 80 tables. St. Louis: C. V. Mosby Company, 1938. \$10.00.

In this book the author presents an admirable summary and digest of the present state of our knowledge of cancer of the breast. Every aspect of the subject is thoroughly reviewed, in all there are more than 3700 references to the literature. The author's own considerable experience is included, particularly in the sections devoted to operative treatment, radiation and end results.

The volume contains little that is new or unusual, but it should be very useful as a reference work to students, teachers and surgeons.

*Physiological Chemistry. A textbook for students.* By Albert P. Mathews, Ph.D. Sixth edition. 8°, cloth, 1488 pp., with 112 illustrations. Baltimore: Williams & Wilkins Company, 1939. \$8.00.

Today, in a great many respects, the biological sciences and biochemistry are transforming medicine into a science. Certainty is thus replacing the art of guessing in diagnosis and treatment of disease. So far, a considerable number of texts have been presented in the field of biochemistry. The majority of the American books are excellent digests of the subject, and the numerous reprints bring the field of biochemistry fairly well up to date. The book written by Mathews is most readable, and fortunately the subject is given in a way that is easy to understand. To each section is added an excellent bibliography. This book combines the subjects of biochemistry and physiology more closely than do some of our

American books. The present edition is greatly improved over the previous editions, and the reviewer can find nothing but praise for it.

*Human Helminthology.* By Ernest Carroll Faust, M.A., Ph.D. Second ed. 8°, cloth, 780 pp., with 302 illustrations. Philadelphia: Lea & Febiger, 1939. \$8.50.

This book, well known to and favorably considered by parasitologists, now appears in a thoroughly revised and enlarged edition. The general arrangement closely follows that employed in the first edition. A valuable addition, particularly for the physician and the medical student, is the section on anthelmintics. An extensive and carefully compiled bibliography makes up the final chapter, a departure and improvement over the earlier publication. The book is pleasantly free from typographical errors and is well indexed. The illustrations are, as a rule, excellent, but to those familiar with the literature, many of the "adaptations," "original adaptations" and "originals" appear to be line drawing copies of original figures. It is apparent that only a very small portion of Figure 73 (page 182) is original.

Contrary to current opinion, *Taenia confusa* is held to be distinct from *T. saginata*. Unfortunately, neither discussion nor mention of the careful morphological study by Anderson on the matter, in which it is concluded that *T. confusa* is a variation and synonym of *T. saginata*, is made in the text, although its reference is included in the bibliography. According to Figure 169 (page 323), echinococcosis in man and reservoir hosts exists from "border to border and coast to coast" in the United States, thus giving the impression that this is one of our major problems in parasitology exceeding that of hookworm, similarly illustrated in Figure 214 (page 428), however, according to Magath's survey, the situation is not alarming, for only 22 of 482 human infections reported from 1808 to 1937 were acquired in North America, namely, in Canada and in the United States.

The book presupposes some previous knowledge of parasitology. It will continue to be a preferred textbook for advanced courses in this subject and a valuable desk reference for physicians.

*Ways to Community Health Education.* By Ira V. Hirsch, C.P.H., A.M. The Commonwealth Fund. 8° cloth, 306 pp., with 85 illustrations. New York: Oxford University Press, 1939. \$3.00.

This volume discusses in detail the various methods of conducting educational campaigns in public health. In the introduction the author states, "The final test of health education is not how much information is distributed but the extent to which behaviour is influenced." Throughout the volume he has discussed the methods used to accomplish this objective. Special chapters are devoted to the public meeting, the newspaper, the radio, the exhibit, and the motion picture. Examples of existing programs are discussed, among these is the Co-operative Cancer Control Committee Program in Massachusetts.

In the appendix a composite picture of a local program of health education is outlined by the health commissioner of a middle sized southern city. The appendix also contains sources of material for public health education and suggestions regarding the purchasing of printing. Bibliographies for further reading are appended to the various chapters.

This book should be of material value to the workers in public health education and of considerable interest to physicians and others desirous of keeping abreast of the trends of this subject.

# The New England Journal of Medicine

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VOLUME 223

AUGUST 15, 1940

NUMBER 7

## HYPOVITAMINOSIS OF ALL FAT-SOLUBLE VITAMINS DUE TO STEATORRHEA\*

### Report of a Case

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BOSTON

IT IS well recognized that steatorrhea may be associated with hypocalcemia and tetany. Two explanations have been offered for this phenomenon. It has been stated that the unabsorbed fatty acids form insoluble calcium soaps in the intestines, thus preventing absorption of calcium. The second and more probable explanation holds that vitamin D being fat soluble, is dissolved in the unabsorbed fat, and that the patient as a result suffers from vitamin D insufficiency. In favor of this hypothesis is the fact that absorption of calcium can be brought to normal in patients with steatorrhea by the administration of large amounts of vitamin D and with no other change in the regime.<sup>1</sup> If one accepts the second explanation the question immediately arises whether such a patient would not be predisposed to insufficiency of all the fat-soluble vitamins. It is the object of this paper to report a case of fatty diarrhea in which there was an insufficiency of at least three of the fat-soluble vitamins, and to emphasize the importance of treating such patients with all the fat-soluble vitamins rather than with vitamin D alone.

### CASE REPORT

M. L. (No. 214,067) aged 35 the wife of a physician entered the Baker Memorial Hospital in September, 1939 on the advice of Dr. Henry H. Haft of Syracuse, New York, because of uncontrolled tetany of 1 month's duration. She had been suffering from abdominal cramps and diarrhea off and on for 7 years. The underlying condition all that time had been a regional ileitis. She had undergone four abdominal operations: an ileocolostomy in 1933, resection of the terminal ileum with anastomosis of the ileum to the cecum in 1933, eradication of the ileocecostomy opening and removal of part of the

cecum in 1933 and resection of 25 cm. of the ileum, followed by side-to-side anastomosis, in 1936. The first two operations were performed at the Mayo Clinic the third and fourth at the Mount Sinai Hospital in New York City.

During the summer of 1939 the patient felt comparatively well. She was having two to three bowel movements a day these were seldom formed. In August she had a recurrence of severe abdominal cramps and an exacerbation of the diarrhea. After several days of this she developed the classic symptoms of tetany. These persisted in spite of large doses of dihydrotachysterol (A.T. 10) and the patient was brought to Boston.

The following points in the past history are of interest. In 1936 at the Mount Sinai Hospital a diagnosis of primary anemia was made. Since that time the patient had been taking intramuscular liver extract once weekly. She had had amenorrhea since December 1938.

The positive findings on physical examination were a sallow complexion, an anxious appearance, marked undernutrition, gums which were bleeding in several spots but were not spongy, a few black-and-blue spots, clubbing of the fingers and toes, a strongly positive Chvostek sign and numerous abdominal operative scars. The tongue was normal. The pelvic and rectal examinations were essentially negative. The blood pressure was 110/80.

The urine gave a + test for albumin, and the sediment showed numerous red blood cells. The stools contained a large amount of fat but no occult blood. The hemoglobin was 14.4 gm. per 100 cc., the red-cell count 3,900,000 and the white-cell count 10,200. A smear of the blood was normal. Gastric analysis showed free hydrochloric acid. The total plasma cholesterol was 1335 mg. per 100 cc. and the ester fraction 88.8 mg. Roentgenograms revealed the presence of gallstones and a considerably shortened small intestine, with areas of active or healed ileitis. A motor meal did not pass through the ileum with excessive rapidity.

The diagnosis on admission seemed quite straightforward. The patient apparently had or had had regional ileitis, which had in some way led to steatorrhea, this in turn had resulted in vitamin D insufficiency (see above) and hence in tetany. The serum calcium was low, 7.0 mg. per 100 cc. (normal about 10.0 mg.). The corresponding serum inorganic phosphorus was normal, 4.1 mg. per 100 cc. The serum protein was low, 4.6 gm. per 100 cc. The serum chloride was 94.7 milliequiv. per liter (normal

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about 1010 milliequiv), and the serum carbon dioxide combining power was 21.7 milliequiv per 100 cc. (normal about 26.0 milliequiv).

The only unexplained findings were the bleeding gums and the red cells in the urine. The plasma-ascorbic acid content was within the normal range, 0.53 mg per 100 cc. A bleeding diathesis was suspected. The bleeding time was found to be normal, 3 minutes. The clotting time, however, was extremely abnormal, there being no clotting at the end of 90 minutes. An associated vitamin K deficiency was therefore considered, and the plasma prothrombin was found to be only 13 per cent of normal. This was the second lowest value that had been obtained in the laboratory. The patient was therefore thought to be suffering from a second, fat-soluble vitamin deficiency. The plasma fibrinogen level was normal. Interestingly enough, on the day following the finding of this alarmingly low prothrombin level, the patient started having numerous subcutaneous hemorrhages over the entire body, and the red-cell count started to fall rapidly.

The possibility of a deficiency in the fat-soluble vita-

cortex and from the male gonads, from an endocrinological point of view the determination is, therefore, an index of the activity of the adrenal cortex and of the male gonads. It is a relatively new test, and there are still many questions which must be answered concerning it. This patient, however, showed none of these steroids in the urine. The only endocrine conditions to date which have shown similar findings are underfunction of all the elements of the anterior pituitary gland and Addison's disease in females. In extreme malnutrition, such as one sees with anorexia nervosa, one expects low values (from 1.0 to 3.0 mg every 24 hours), but not an absence of the steroids in the urine, that is, the excretion of less than 0.5 mg every 24 hours.

The amenorrhea was of course not surprising in view of the marked malnutrition. There was no excess of follicle-stimulating hormone in the urine, which indicates that the ovarian hypofunction was secondary to a pituitary hypofunction rather than to a primary disturbance in the ovaries.

Inasmuch as the patient had difficulty in absorbing

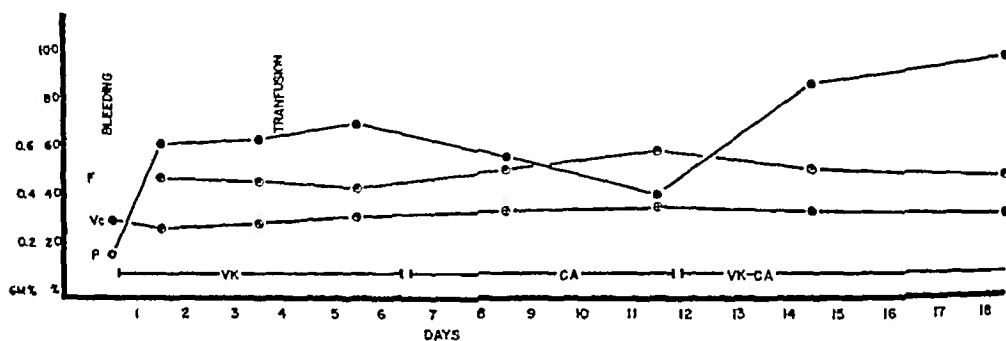


FIGURE 1 Results of Coagulation Study on M. L.

Line VK represents the period during which 1 mg vitamin K (methyl naphthoquinone) was given daily, and line CA 9 gr deoxycholic acid daily, curve P represents the plasma prothrombin levels in per cent, curve Vc the hematocrit readings in per cent, and curve F the plasma fibrinogen levels in grams per 100 cc.

min A was then considered. Dr. John F. McCreary and Dr. Charles D. May, of the Children's Hospital (Boston), carried out the necessary determinations. They found 8.2 units of vitamin A per 100 cc. of serum (normal, 10 to 20 units), and 0.77 units of carotenoids (normal, 30 to 80 units).<sup>2</sup> While the vitamin A content was low, it was not sufficiently so in Dr. McCreary's opinion to cause clinical symptoms. It should be noted, however, that the patient had had cod liver oil for 2 weeks before admission. The carotenoids, furthermore, which are a precursor to vitamin A, were extremely low. The patient on admission had no symptoms which could be ascribed to vitamin A deficiency. She was not tested for dark adaptation. There was no hyperkeratosis pilaris. Shortly after admission, however, she developed an eruption on the breast and abdomen which Dr. Jacob Swartz diagnosed as xeroderma. This condition is thought to be due to vitamin A deficiency.

The possibility of a deficiency of the fourth fat-soluble vitamin, vitamin E, was considered, but no specific tests were carried out.

Inasmuch as steroids are fat-soluble, it seemed possible that the patient had an associated disturbance in steroid metabolism. It was therefore decided to determine the quantity of 17-ketosteroids in the urine by the method of Callow.<sup>3,4</sup> By this designation is meant the steroids with a ketone linkage on the 17th carbon atom, for practical purposes this means the steroids derived from the adrenal

fat, the first therapeutic consideration was obviously a low-fat diet. Secondly, it was apparent that the various fat-soluble vitamins should if possible be administered in some vehicle other than oil. Where that was impossible it was preferable that they be given in as concentrated a preparation as feasible, so that the absorption of a very small amount of fat would result in the absorption of a large amount of vitamins.

Vitamin D was given in the form of Drisdol (Winthrop Chemical Company), in which the vitamin D<sub>2</sub> is dissolved in propylene glycol.\* The patient was started on 500,000 USP units daily. The tetany responded readily to this treatment, and the serum calcium rose from 7.1 to 10.0 mg per 100 cc. during a period of 3 weeks. The serum phosphorus level also rose from 4.1 to 5.1 mg. per 100 cc., and the serum protein from 4.6 to 6.4 gm.

The vitamin K deficiency was treated by the oral administration of 1 mg of 2-methyl-1,4-naphthoquinone in castor oil and 9 gr of deoxycholic acid daily†. The plasma prothrombin concentration, as determined by a modification of the two-stage method of Warner, Brinkhous and

\*We are indebted to Mr. C. B. Taft of the Department of Medical Research, Winthrop Chemical Company, New York City, for having prepared an especially concentrated vitamin D<sub>2</sub> preparation in propylene glycol.

†The methyl naphthoquinone was kindly supplied by Dr. A. Black of the Squibb Research Laboratory, E. R. Squibb and Sons, New York City, and the deoxycholic acid by Riedel-de Haen, Incorporated, New York City.

Smith<sup>8</sup> rose rapidly and within 24 hours the concentration was 60 per cent of normal and the bleeding tendency was under control (Fig 1). From the 1st to 7th days the methyl naphthoquinone was given without deoxycholic acid, and this sufficed to maintain the prothrombin concentration at a safe but still abnormally low level. During the second 6-day period deoxycholic acid was given without methyl naphthoquinone, with a resultant gradual fall in prothrombin concentration. Finally, when both drugs were given together the prothrombin level rapidly rose to 100 per cent, the normal value. In Figure 1 are shown the values for prothrombin, fibrinogen and red-cell hematocrit during treatment. These findings suggest that the patient's ability to absorb fat soluble substances had not been entirely lost but was markedly reduced. Adequate absorption took place when deoxycholic acid was taken into the gastrointestinal tract.

Vitamin A was given in the form of Lederle's Vi-Delta liquid concentrate. Each gram of this preparation contains 90,000 U.S.P. units of vitamin A and 11,200 U.S.P. units of vitamin D. The patient received 45 drops of this preparation daily. The vitamin A content of the serum rose from 8.2 units on October 4 to 36.0 units on October 19 (normal 10 to 20 units) and the carotenoids during the same time rose from 0.77 to 6.5 units (normal 30 to 80 units). There was a definite improvement in the xeroderma during this period.

In spite of the fact that no evidence of vitamin E deficiency had been demonstrated it was considered advisable to treat the patient with this vitamin and she received 2 cc. daily of wheat germ oil (Squibb).

In addition to the above-mentioned treatment she received one transfusion and 5 mg. of vitamin B<sub>1</sub> (thiamin chloride) subcutaneously each week. There was probably no real indication for thiamin chloride.

The result of therapy was most dramatic. The overcoming of the tetany and of the bleeding diathesis has already been discussed, as has the improvement of the xeroderma. The most striking change, however, was in the general appearance of the patient. From an individual in a very critical condition who did not want to live she changed to a quite healthy-appearing young woman with a very optimistic outlook on life. Until her 17th day in the hospital, October 2 she had been too ill to be weighed. On that date her weight was 85 pounds and she was definitely convalescing. On discharge 18 days later the weight was 93 pounds. There was also some improvement in the gastrointestinal symptoms. There were fewer bowel movements a day and each was less watery; she likewise had fewer cramps. On discharge the 17 ketosteroids were still absent from the urine.

The patient returned for a follow-up examination on January 24, 1940, having continued the treatment at home. She was markedly improved. Her weight had increased to 123 pounds, and she had had two menstrual periods. She continued to have two or three bowel movements a day. Examination of the stools showed no fat while on a low fat diet. The serum calcium was 9.8 mg. per 100 cc., the serum phosphorus 4.0 mg., and the serum protein 6.8 gm. In 100 cc. of serum there were 26.5 units of vitamin A and 18.3 units of carotenoids. The plasma prothrombin concentration was 100 per cent. There were 2.0 mg. of 17 ketosteroids per 24 hour urine specimen.

#### SUMMARY AND CONCLUSIONS

A case history is presented to bring out a certain cause-and-effect relation which must not in

frequently be met with and which brings up certain important therapeutic considerations.

The various complications in the case reported were thought to bear the following relations to each other. Chronic regional ileitis was presumably the initial lesion and probably had no connection with the cholelithiasis, but did lead to insufficiency of the intestines as an organ, this resulted in a marked steatorrhea, which in turn prevented the absorption of all the fat-soluble vitamins, there resulted, therefore, hypovitaminosis D with hypocalcemia and tetany, hypovitaminosis K with a severe bleeding diathesis and a failure of the blood to clot, hypovitaminosis A with a low serum content of carotenoids, the precursor of vitamin A, and xeroderma and probably hypovitaminosis E, although there was no clinical or laboratory evidence of this condition. It is also possible that the steatorrhea led to the disturbance in the steroid metabolism which resulted in an absence of 17-ketosteroids from the urine. Furthermore, because of a deficiency in the protein metabolism, the patient developed a pituitary amenorrhea with an absence of follicle-stimulating hormone in the urine. Finally, the intestinal anastomoses that were necessitated also led to a primary anemia similar to that in the cases reported by Barker and Hummel,<sup>4</sup> in spite of the presence of free hydrochloric acid in the gastric contents.

It is emphasized that pan fat soluble vitamin deficiency should be looked for in all cases with chronic steatorrhea, regardless of the presenting symptom.

Patients with chronic steatorrhea should receive a low fat diet, and where possible should obtain fat-soluble vitamins in fat-free vehicles.

The vitamin K deficiency in this case responded dramatically within twenty-four hours to the oral administration of 1 mg. of 2 methyl 1, 4 naphthoquinone in corn oil the plasma prothrombin concentration rising from 15 to 60 per cent of normal.

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## RECOVERY FROM ACUTE RHEUMATIC FEVER WITHOUT PERMANENT CARDIAC DAMAGE\*

MORTON G. BROWN, M.D.,† AND LOUIS WOLFF, M.D.‡

BOSTON

THE relation between the occurrence of rheumatic fever and the development of permanent cardiac lesions has been recognized for over a century. Until recently, however, those patients in whom no evidence of permanent cardiac damage could be detected have not been studied systematically. The purpose of this paper is to call particular attention to patients who, even in spite of repeated and severe attacks of rheumatic infection, present no clinical or laboratory evidence whatever of permanent cardiac damage following recovery from the active infection.

### MATERIAL

This study is based on 175 consecutive, unselected patients admitted to the wards of the Beth Israel Hospital with acute rheumatic fever, with or without chorea. Only the patients in whom the diagnosis was clear were included. Following the acute attack, they were seen in the Cardiac Clinic of the Outpatient Department on repeated occasions over periods of time varying between four and eleven years, and most of them were seen by us for the final evaluation of their cardiac status. In arriving at the final opinion, the physical examination, the electrocardiogram, the seven-foot x-ray film of the heart and the fluoroscopic examination for chamber enlargement were taken into consideration.

### CLINICAL OBSERVATIONS

In this series of 175 cases, there were 89 patients who developed or already had valvular damage as a result of rheumatic fever. Patients presenting loud and constant systolic murmurs as the only cardiac abnormality were included in this group. The cases with organic cardiac damage differed in no way from similar ones already reported, and will not be discussed further.

The remaining 86 cases were divided into three groups (Table 1). Group 1 included 21 patients who at no time showed murmurs or other evidence of cardiac involvement. Group 2 consisted of 29 patients in whom, at the time of rheumatic activity, murmurs and other evidences of cardiac involvement were present but subsequently dis-

appeared. Group 3 included 36 patients who showed a persistent but inconsequential systolic murmur.

In Group 1, the rheumatic fever did not appear to differ clinically from that in the other two groups, it was just as severe, the associated fever was as great, the duration of illness was as long and the recurrences seemed to be as frequent. The

TABLE 1 *Classification of 175 Consecutive, Unselected Cases of Acute Rheumatic Fever According to Cardiac Damage*

CLASSIFICATION	No. of Cases	Per Cent
Valvular heart disease	89	51
No evidence of heart disease	86	49
Group 1 no murmurs	21	12
Group 2 murmurs disappeared	29	16
Group 3 systolic murmurs persisted	36	21
Total	175	

average age at the time of the first attack was fourteen, and the follow-up period averaged six and a half years. Eight patients had multiple attacks.

In Group 2, the average age at the time of the first attack was fourteen, and the follow-up period averaged eight years. Thirteen patients had mul-

TABLE 2 *Data on the Disappearance of Murmurs in 29 Cases of Acute Rheumatic Fever*

DATA	No. of Cases
Systolic murmur disappeared	18
Systolic murmur became inconstant	4
Apical systolic and diastolic murmurs disappeared	6
Apical systolic and diastolic and aortic diastolic murmurs disappeared	1
Total	29

multiple attacks. Six had electrocardiographic changes, such as a lengthened PR interval or abnormalities of the T waves or the ST intervals. Three showed an enlarged heart by x-ray and 3 had pericarditis. All these evidences of cardiac injury, as well as the murmurs, subsequently disappeared. The type of murmur is shown in Table 2. Of the 6 patients who had apical systolic and diastolic murmurs, only 3 had enlarged hearts by x-ray at the time the murmurs were present.

In Group 3, the murmurs were such that they would have been regarded as functional but for the history of rheumatic fever. In several cases the murmur was known to have existed prior to the first attack of rheumatic fever, following which it did not change. It is possible, of course,

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that there was previous unrecognized rheumatic infection. In all cases the murmur was soft and faint, and varied even to the point of disappearance with respiration or position. The average age at the time of the first attack was thirteen, and the follow up period averaged seven years. Eighteen patients had multiple attacks. As in Group 2, there were patients who showed other evidence of cardiac involvement at the time of activity. Seven had electrocardiographic changes, 3 had enlarged hearts by x ray and 3 had pericarditis. At the last examination all 36 patients had normal sized hearts and were symptom free, and the fluoroscopic and electrocardiographic examinations gave normal results. While some patients may have minimal changes in the endocardium the signs did not warrant a diagnosis of valvular deformity and the group as a whole must be regarded as free from heart disease. The clinical evidence of rheumatic fever was not different in respect to severity, duration or recurrences from that seen in the patients whose hearts remained permanently damaged.

#### COMMENT

It is known that some patients with acute rheumatic fever escape permanent organic valvular damage.<sup>1-3</sup> The present study confirms this fact in a striking manner, and indicates that the incidence of those escaping permanent cardiac damage—50 per cent—is higher than that in any other published series.\* It is generally believed that the more severe the infection or the greater the number of recurrences, the more apt is the patient to develop permanent cardiac injury. This belief, however, is not substantiated by the findings here reported. The rheumatic infection in the patients who recovered without permanent heart disease was no different clinically from that in the others, being just as severe in its manifestations and in its evidences of serious heart involvement, that is, cardiac enlargement, pericarditis and electrocardiographic changes. There was no difference in the measurable duration of the rheumatic activity or in the incidence of cases with multiple attacks. Although the average age at the time of the first attack was somewhat higher in this series than in those reported elsewhere, 35 patients were under ten at the time of their first rheumatic infection.

Of the 86 patients who escaped permanent cardiac damage, 42 had multiple attacks of rheumatic fever. It would appear, therefore, that patients

who recover without permanent organic heart changes from a first attack have an excellent chance of doing so from subsequent ones. This conclusion is similar to that recently reached by Boone and Levine.<sup>4</sup> This fact is of important prognostic and therapeutic significance, and makes possible the less rigid restriction of activity of certain patients during subsequent attacks of active rheumatic infection.

Those patients in whom, following an attack of rheumatic fever, a soft inconstant systolic murmur persists without other evidence of heart disease present a difficult problem for evaluation. Although recent reports indicate that some of these patients may develop signs of valvular deformity many months or years after a rheumatic infection, they do not state whether the patients were completely free of murmurs in the intervening years. In the present series, during follow-up periods of observation averaging seven years, none of the patients with persistent systolic murmurs showed evidence of progressive valvular involvement. In other cases all murmurs disappeared during the follow-up period. This finding is similar to the observations of other authors.<sup>4-6</sup> Inasmuch as several patients had normal sized hearts by x ray at the time the murmurs were present, it would appear that cardiac dilatation is not the sole explanation for the disappearance of murmurs. Since the physical signs can change, it is necessary to delay for several years the final evaluation of the status of the heart following an attack of rheumatic fever.

#### CONCLUSIONS

Fifty per cent of a group of 175 patients with acute rheumatic fever showed no evidence of heart disease after follow up periods averaging seven years.

There is no constant relation between the severity of the illness or the number of recurrences and the development of cardiac damage.

Patients who show no permanent organic heart changes following the first attack of rheumatic fever are prone to escape permanent injury despite further attacks.

The final evaluation of the state of the valves must be delayed for several years after an attack of rheumatic fever.

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\*It should be noted that the average age at onset of rheumatic fever in our patients is higher than that in some of the series reported by other authors. Most observers, we believe, would attribute the great incidence of complete and permanent cardiac recovery in our cases to this factor. The relation between permanent cardiac damage and the age of onset of rheumatic fever is being investigated and will be reported in a separate communication.

## INFECTIONS OF THE UPPER URINARY TRACT IN THE DIABETIC PATIENT\*

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IN AN earlier publication from the George F Baker Clinic, Sharkey and Root<sup>1</sup> reported that 18 per cent of 196 diabetic patients examined post mortem showed serious infection of the urinary tract. This paper presents further studies based on 86 cases of infection of the kidneys and on 143 autopsies of diabetic patients encountered in the period 1934-1939.

### ETIOLOGY

If diabetes should be suspected in the presence of a carbuncle, it should be sought as a factor also in acute or chronic renal infection. Diabetic renal infections are excessively frequent, and present special difficulties in diagnosis and treatment.

Certain basic characteristics of diabetes predispose to the development of infections of the urinary tract. Glycosuria itself favors the persistence and multiplication of pathogenic organisms in the urinary tract. Secondly, in patients with uncontrolled diabetes the excessive excretion of the nitrogenous products of protein catabolism adds further nutrient material for the urea-splitting organisms. Ketonuria, a factor antagonistic to the growth of some of the pathogenic organisms in the non-diabetic subject, fails to exert any apparent therapeutic effect on acute renal infections during diabetic acidosis. Indirectly, glycosuria, by causing pruritus vulvae and its attendant local traumatization, favors in women the direct invasion of the urinary bladder.

Consequent on the frequency of infections of the skin, diabetic patients have a higher incidence of septicemia, particularly due to organisms of the staphylococcal group. Positive blood cultures are common in severe diabetic sepsis, and in a hospital dealing to a large extent with diabetic patients, positive cultures far outnumber those reported in general hospitals. The frequency of renal cortical abscess in such septicemias is striking. Some special local susceptibility, such as may be caused by the presence of glycogen deposits in the renal tubules, may exist in addition to the anatomical vulnerability of renal structure, allowing the organisms to

gain a foothold. Bacteria are notoriously prone to attack damaged structures.

Finally, uncontrolled diabetes is a cause of various neuropathic conditions, usually termed diabetic neuritis, one of which may produce disturbances in innervation, culminating in "cord bladder." This special cause of infection of the urinary tract is particularly difficult to treat. Though the mechanism is unknown, it is most probably a degeneration of the central nervous system of a reversible sort, as evidenced by the high total protein of the spinal fluid in many cases. Seven cases from this clinic were reported by Jordan and Crabtree<sup>2</sup> in 1935.

Paralysis of the bladder is seen occasionally in young patients of both sexes with uncontrolled glycosuria. It occurs most frequently in cachectic, neglected diabetic women with prolonged infection and gangrene of the lower extremities, who may present retention of urine from the time of hospital entry.

The majority of diabetic patients in this study presented other potential causes for renal infection, which may be grouped as the common local and systemic degenerative effects of age. These include old perineal lacerations with cystocele formation in women, prostatic hypertrophy and malignancy in men, neoplasms of other portions of the urinary tract, calculi, nephrosclerosis and, usually, diminished circulatory efficiency of varying degree. Although these predisposing factors are not truly peculiar to the diabetic patient, they assume greater significance in view of the previous discussion of the essential peculiarities of the diabetic state.

### DIAGNOSIS

Deep infection in the diabetic patient, as in or about the kidney, often fails to arouse the classic local and systemic manifestations. Fever, leukocytosis and localizing tenderness and muscle spasm may be absent or equivocal in a patient with nausea and vomiting, poorly defined abdominal pain and marked glycosuria. The urinary sediment may be misleading. Nevertheless, early diagnosis is essential, especially of the side involved, if the patient is to recover.

A detailed history is usually the best single guide in the problem. Repeated careful biman-

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ual palpation will often reveal increase in kidney size. Heavy percussion in the costovertebral angles may help in localization through the acute pain produced. Finally, x-ray evidence of calcification, change in kidney outline, psoas muscle spasm and pyelographic studies are of invaluable aid. However, the carrying out of retrograde pyelograms may be hazardous in a sick patient, and gaseous distention and reduced renal function render the intravenous method unsatisfactory. Occasionally, after a period of close watching, an exploratory flank incision must be made for abscess drainage or whatever procedure is indicated. Such an operation may be as justified and life saving as a laparotomy for an acute condition of the abdomen. The following case exemplifies the difficulties in point.

**CASE 2008.** A 48-year-old clothing merchant, diabetic for 16 years, entered the hospital complaining of severe pain of 1 month's duration, radiating down the right thigh. He had had a carbuncle of the neck treated at another hospital 5 months previously, one of two blood cultures taken at that time was positive for staphylococci. Because of the pyuria he had had cystoscopy and retrograde pyelography 2 months previously and to this he attributed the pain in the right leg. Four centrifuged specimens of urine showed only 0 to 17 white blood cells per high power field, and although he had fever an elevated white cell count and, later, chills, there were no localizing signs. Equivocal tenderness in the kidney region finally became definite on the left, and retrograde pyelograms showed a mass at the upper pole of the left kidney from which, 3 weeks after entry, a large amount of pus containing hemolytic *Staphylococcus aureus* was drained. By this time, however, the patient had developed a true acute septicemia due to the same organism and of this he died 2 days later.

Probably the process in this case dated from the time of the first carbuncle five months previous to admission. The patient's life might well have been saved by operation performed before the onset of septicemia. We are led to this opinion by the fact that operations for acute renal suppuration or perinephric abscess in 13 cases of this series resulted in recovery in 9.

#### TYPES OF RENAL INFECTION

Classification into hematogenous and ascending types of renal infection has been attempted by means of the following criteria. Hematogenous infections were defined as occurring in patients previously without urinary symptoms or pathologic urinary sediment in whom there was a history of a distant primary infected focus, with or without bacteriological evidence of invasion of the blood. Such cases presented no evidence of a previous cystitis or prostatitis. Under ascending infections were included cases with a history of previous disease of the urinary tract, with

pyuria and evidence of mechanical obstruction, with or without gross changes in the drainage system revealed by pyelography.

#### RENAL INFECTIONS AT AUTOPSY

The statistical survey of 3000 routine autopsies by Ophüls<sup>2</sup> in a large general hospital has been used to establish the frequency of serious renal infection in the population at large. Four per cent of the cases were found to have sepsis of the upper urinary tract. Diabetes was present in only 1 per cent of the 3000 cases. Of the 123 cases with infection of the upper urinary tract, 19 (15 per cent) represented metastatic abscesses, a majority of which were secondary to septic endocarditis. One hundred and four cases (85 per cent) showed ascending infection of the urinary tract, of which an eighth were associated with stone, a quarter were secondary to bladder paralysis and a third were the result of prostatic hypertrophy.

The present series consists of 143 autopsies of diabetic patients performed under the supervision of Dr. Shields Warren at the New England Deaconess Hospital between August, 1934, and August, 1939, of which 31 cases (22 per cent) showed kidney infections. Of these, 12 (38 per cent) represented metastatic processes, secondary to major skin infections in 6 cases and secondary to septic endocarditis in none. Eighteen cases (58 per cent) were the result of ascending infection, which, almost without exception, was generalized in type. In 1 case the type of infection was not determined.

From the same clinic in 1935 Sharkey and Root<sup>1</sup> published a series of 35 purulent renal infections discovered in 196 autopsies on diabetic patients between 1919 and 1934, 26 (74 per cent) were hematogenous, 5 (14 per cent) were ascending and the nature of 5 was unknown.

A comparison of the Ophüls and the Sharkey and Root series and our own is shown in Table I.

TABLE I The Incidence of Infection of the Urinary Tract in Three Autopsy Series

Series	Number of Autopsies	Type of Case	Infection of Urinary Tract	No. of Cases Cured
Ophüls <sup>2</sup> (1925)	3000	General	123	4
Sharkey and Root (1914-1934)	196	Diabetic	35	18
Baldwin and Root (1934-1939)	143	Diabetic	31	22

It will be seen that serious renal infections were found at autopsy to occur five times as frequently in the diabetic as in the general group.

#### COMBINED AUTOPSY AND CLINICAL MATERIAL

Study of the files of the George F. Baker Clinic from August, 1934, to August, 1939 discloses a

total of 86 cases of renal infection in diabetic patients. Subtracting the 31 autopsied cases and the 6 additional deaths without postmortem, there remain 49 patients, or more than one half, who recovered from their infection sufficiently to leave the hospital. However, 22 of these cases were diagnosed as pyelitis, leaving 27 with non-fatal purulent parenchymal involvement as opposed to the 37 fatal cases. This gives for the total of 64 cases of parenchymal renal infection a mortality of 58 per cent.

Of the 64 cases with parenchymal involvement, 16 (25 per cent) were hematogenous infections and 47 (73 per cent) were ascending infections, 1 was unclassified (Table 2). The high mortality

TABLE 2 *Results of Parenchymal Renal Infection in 64 Diabetic Patients*

RESULTS	ASCENDING INFECTIONS		HEMATOGENOUS INFECTIONS		UNCLASSIFIED INFECTIONS	
	NO OF CASES	PER CENT	NO OF CASES	PER CENT	NO OF CASES	PER CENT
Died	21	45	15	93	1	100
Recovered	26	55	1	7	0	0
Totals	47		16		1	

of the hematogenous type, 93 per cent, is a challenge to earlier diagnosis and operation.

The above figures indicate the possibility of recovery for patients with severe kidney involvement even though diabetic. In 19 cases of ascending renal infection arrest or cure occurred, usually by means of some major surgical procedure, that is, in the above group there were 3 cases with nephrectomy, 2 with nephrostomy, 2 with ureteral lithotomy, 3 with drainage of an abscess and 3 with stricture dilatation. On the other hand, such procedures may be only ameliorative and at least 1 of the cases (No. 3683) receiving nephrectomy subsequently developed infection of the opposite kidney and died from uremia eight years later.

#### SEX

In the hematogenous group, the sexes were equally represented. However, there were nearly twice as many females as males in the ascending infection group. This difference may be due to the greater incidence of diabetes in women in the later age group and the greater number of diabetic girls and women admitted to the clinic. In part, however, it represents the increased susceptibility of the female urinary tract to infection for anatomical reasons, which include the short distance from the urethral meatus to the bladder and the close proximity of the vaginal flora.

#### AGE

The frequency of blood-borne infections is a rather constant one at all ages. The ascending infections show a slow rise for the first five decades to the age of fifty, when the frequency suddenly rises abruptly for two decades, probably owing to the influence of prostatism, cystocele, calculi and so forth, to fall again at seventy years.

#### DURATION AND CONTROL OF DIABETES

Wide variations in the duration of diabetes are to be found, from two months to twenty-three years, so that no direct correlation can be made. The greater the duration of the disease, the older the patient and the more advanced the degenerative vascular changes, the lower is the resistance of the patient. On the other hand, it must be concluded, as did Sharkey and Root,<sup>1</sup> that increased susceptibility to infection is developed soon after onset of diabetes.

The influence of control of diabetes is in part directly reflected in the development of boils, carbuncles or other primary sources of infection leading to septicemia, a special danger in diabetic coma.

#### URINARY OBSTRUCTION

Calculi in the upper urinary tract were present in 14 of the 47 cases of ascending infection, again with an incidence in females nearly twice that in males. It is often difficult to know whether infection or stone formation developed first, since each may initiate the other. Obstruction due to hypertrophy of the prostate, new growths, malignant and benign, and stricture were all represented in a total of 10 cases and paralysis of the bladder in 3 cases, leaving 20 cases (43 per cent) in which no mechanical cause was evident.

#### PYELITIS

The 22 cases of pyelitis collected from 1934 to 1939 emphasize an important point, namely, that pyelitis often represents in the diabetic patient the inception of a purulent renal lesion. The practice of catheterization postoperatively and in diabetic coma to obtain specimens of urine as a guide to insulin therapy is a dangerous one. Regardless of the precautions taken, the chance of introduction of infection is great. At least 3 juvenile diabetic patients in this series developed acute pyelitis, which directly or indirectly contributed to their death, following such a procedure. For the management of cases of coma, resort should be made to frequent determinations of the chemical constituents of the blood. When reten

tion of urine occurs, the use of synthetic parasympathetic stimulants, such as Doryl, has been effective in some cases. In this connection, it is possible that low spinal anesthesia by novocain may disturb the neurologic mechanism of bladder control, particularly in the presence of chronic cystitis. Possibly the same results would be obtained with inhalation anesthesia. The answer to the question remains unsettled. Cases of neurogenic dysfunction of the bladder following spinal anesthesia are reviewed by Pearson and Twomey<sup>11</sup> who report a recent case. Their patient, a sixty-year-old man, developed complete retention of urine after spinal anesthesia, which was finally relieved by resection of the presacral nerve.

Pyelitis is regarded by some clinicians and pathologists (Boyd<sup>4</sup>) as always associated with some parenchymal involvement of the kidney, that is, a pyelonephritis of mild degree. This may be an extreme view, but the condition in some cases is certainly the beginning of a chronic infection particularly if there is an anatomic fault that favors stasis. On the other hand, many patients receiving adequate treatment apparently recover. In Case 6287, a diabetic dwarf with pulmonary tuberculosis had clinical pyelitis in 1935 under hospital observation, yet an autopsy in 1939 showed no signs of kidney infection, though chronic cystitis was present.

### BACTERIOLOGY

For staphylococci as well as for streptococci ability to produce hemolysis in a blood agar plate is one of the most reliable indices of virulence short of actual animal inoculation studies. According to Zinsser,<sup>8</sup> the quantity of hemolysis is approximately proportional to virulence and lethal toxicity. The value of the test for hemolysis by *Staphylococcus aureus* is strikingly borne out in this series.

The organism responsible for acute pyelitis was in a great majority of the cases the colon bacillus, which was obtained in 11 out of 13 cases studied. In 3 cases it was grown in association with *S. albus*. The latter organism according to Schulte<sup>6</sup> at the Mayo Clinic, may be found as a nonpathogenic inhabitant of the normal urinary tract in contrast to *S. aureus*, which is never isolated from the urine of normal subjects of either sex or from the prostatic secretion of normal male subjects. In general, this has been confirmed in our experience. One patient proved to have a *Bacillus proteus* infection, another a hemolytic *S. aureus* infection. In none of the above cases of pyelitis did the patient succumb.

In the patients with parenchymal renal infec-

tion of the ascending type, the colon bacillus was again in predominance, that is, present in 19 out of the 33 cases studied, 4 of the patients succumbing primarily to the kidney complications. Non-hemolytic *S. aureus* was cultured in 8 cases, and of these it was in association with the colon bacillus in 6. The hemolytic form was recovered in 6 cases. In all, the patients were gravely ill, 4 succumbing to septicemia, the other 2 recovered from an almost moribund state, following nephrectomy in one case and following drainage of a pararenal abscess in the other.

The bacteriology of the hematogenous group was quite different from that of the ascending infections. Hemolytic *S. aureus* was cultured in 11 of 13 cases, organisms in the others being non-hemolytic *S. aureus* and the colon bacillus. Of the group with hemolytic *S. aureus* all but 1 patient died of the infection. This fact, taken together with the outcome of the 6 cases cited in the preceding paragraph, establishes the seriousness of any infection of the urinary tract caused by this organism. It also makes imperative long continued follow up treatment for cases of pyelitis developing after catheterization during coma, such as Case 17908, a child of four, in whom this organism was recovered.

The hemolytic *S. aureus* therefore is the *bête noire* of the diabetic patient, and unfortunately in diabetic blood and wound cultures staphylococci are predominately present. It is well known that differences exist in the types of lesions produced by bacteria and that accordingly the host must cope with different situations. Staphylococci by their necrotizing power are self localizing in the nondiabetic subject, but this is not true of the diabetic patient, who is apparently deficient in his power of resistance and unable to throw up a protective inflammatory barrier that will limit the infection and prevent invasion of the blood stream. As a result, in diabetic patients staphylococci act like streptococci.

### TREATMENT

#### General Principles

A few words regarding the methods of study and treatment found useful in the diabetic clinic may be of value. Recently a nurse has been especially assigned to the group of patients with infections of the urinary tract. On a special form she keeps a daily record of microscopic examinations of the urine, four-hour determinations of urinary pH by nitrazene paper, chemical studies of the blood and urine, and drug therapy, including sulfanilamide, mandelic acid and so forth. The indication for catheterization is recorded, as

well as the quantity of urine voided prior to the procedure, the amount obtained by catheter and the time interval between the two, for an accurate determination of residual urine. Culture of the first specimen obtained by catheter with microscopic examination of the sediment is a routine procedure, and is especially important in all postoperative patients with urinary difficulty requiring drainage. Pending the bacteriological report, antiseptic therapy is started orally with 10 gr of methenamine and 10 gr of sodium acid phosphate three times a day, and fluids are forced.

Routine catheterization and the instillation of Mercurochrome at the conclusion of all gynecological operations, as advised by Woodruff and Te Linde,<sup>7</sup> have not been employed. Indeed, in this series no cases were found in which infection of the upper urinary tract had followed an operation.

Cases with paralysis of the bladder require repeated catheterization, tidal drainage or constant drainage with irrigations for varying periods. The last-named is best carried out by a closed system with Y-tube connections to a sterile irrigation flask. Weekly trials for spontaneous micturition should be made while drainage is suspended, with repeated measurement of the residual urine, which should not be allowed to exceed 200 cc in amount. Ultimately with high-vitamin therapy, including particularly the vitamin B complex, good diabetic control and general supportive measures, normal neurologic function often returns. The great necessity in this period of treatment is the prevention of overdistention of the bladder and of acute ascending renal infection, by instituting proper aseptic bladder management, as is illustrated by the following case.

**CASE 18031** A 66-year-old housewife, with diabetes of 8 years' duration, was admitted in a toxic, emaciated, anemic condition with a temperature of 102.4°F, secondary to an extensive infection of the left foot of over 3 months' duration. She was unable to void spontaneously, and after 7 hours was catheterized, 480 cc. being removed. The procedure was repeated twice daily for 3 weeks, at the end of which time constant drainage was instituted. After 3 days of diabetic regulation and hydration, a closed amputation of the left thigh was done under spinal anesthesia, following which there was a drop in the temperature and pulse. A chill occurred on the 10th postoperative day consequent to infection of the stump, which was drained. Pus appeared in the urine, and a culture showed colon bacilli, which were also obtained from the stump wound. After a week on constant drainage with irrigations, repeated attempts were made to eliminate the catheter, fortified by the use of strychnine sulfate and of synthetic parasympathetic stimulants, such as Mecholyl Bromide, 400 mg three times a day, but without avail other than the development of a desire to void. The chemical constituents of the blood were normal, as were the results of lumbar puncture, except for a finding of 140 mg total

protein in 100 cc. of fluid. A second trial with injection of Doryl (0.25 mg), after 10 more days of constant drainage and the use of a vitamin B<sub>1</sub> preparation, finally induced spontaneous voiding, with a gradual decrease in residual urine to 135 cc. The patient was discharged 3 months after entry, taking iron and a urinary antiseptic and walking on a peg leg. Six months later she had gained 25 pounds and had no urinary difficulties.

Mechanical factors of prime importance are cystocele in women and prostatic enlargement in men. In order to rule out some cause for obstruction in the upper urinary tract, it has been customary first to employ excretion pyelography. Because of the extreme danger of introducing a virulent secondary organism or of stirring into activity a latent process by the procedure of ureteral catheterization, retrograde pyelography is done only if the information obtained by excretion pyelography is inadequate. One case in this series followed just such a tragic, prematurely hastened course.

Early consultation with a genitourinary surgeon is essential, and we are especially indebted to Dr. Harvard H. Crabtree for advice in the treatment of these cases. There is every reason to believe, in retrospect, that in nearly every one of our fatal cases the process was so localized at an earlier period that, had operation been performed, the life of the patient might have been saved. This means being alert to the possibilities and learning to recognize the early signs of renal and perirenal involvement, and thus by the establishment of drainage preventing in many cases an overwhelming and fatal infection. Every diabetic patient with a recent purulent infection, such as a carbuncle, should have a monthly health investigation for at least half a year. Serious attention should be paid to any suspicious symptoms.

Urinary calculi should not escape detection. Too often, even today, hyperparathyroidism is overlooked. The latter should be ruled out by studies of the blood calcium and phosphorus, when it has been disproved, a regime of diet should be outlined unfavorable to the recurrence of the stones, based on the chemical nature of the stone removed.

#### CHEMOTHERAPY

All our cases have required chemotherapy, often as an adjunct to surgery. Very rigid standards must be set up for cure, including elimination of pyuria and two negative, catheterized cultures of the urine. Because of the bacteriostatic effect of medication, cultures must not be taken until three or four days after the cessation of therapy. The choice of a drug depends on the organism present, the pH of the urine and the ability of the patient to tolerate the selected drug in effective dosage.

Success depends to a tremendous degree on the absence of stasis.

In the experience of this clinic, no drug has been tried which is effective against the staphylococcus in concentrations that the average patient is able to tolerate. Sulfanilamide and its less toxic derivative, Neoprontosil, have been employed for adults in doses of 15 to 20 gr six times a day, with equal amounts of sodium bicarbonate and restriction of fluid intake to 1500 cc. The frequency of the dosage is important, particularly with Neoprontosil, because of the rapid urinary elimination of 85 to 90 per cent of the drug in four or five hours (Cook<sup>4</sup>). According to Lockwood and Lynch,<sup>5</sup> the presence of the products of tissue destruction completely blocks the effect of sulfanilamide.

Although sulfamethylthiazol and sulfathiazol have recently been used in cases of staphylococcal infections, our experience is too limited to justify an opinion of their effectiveness. Rather encouraging reports (Campbell<sup>10</sup>) concerning the use of neosarsphenamine intravenously have recently appeared. It must be pointed out, however, that the majority of our patients taking the above drugs were gravely ill at the time of inception of treatment, or else had renal mechanical obstruction.

Against the colon bacillus, 30 gr of ammonium mandelate four to six times a day, together with one third this quantity of ammonium chloride, has been a great aid. In cases of pyelitis without obstruction it is often curative. However, ammonium mandelate is useless in urine with a pH higher than 5.5. Therefore when alkalinity persists, despite the use of such acidifying agents as an acid-ash diet and ammonium chloride, trial had best be made with sulfanilamide, which works best in alkaline solutions (Helmholz and Osterberg<sup>21</sup>). Further prolonged unsuccessful acidification therapy, by mobilization and excretion of calcium and phosphorus, may lead to the rapid formation of stone (Chute<sup>13</sup>).

Against the beta hemolytic streptococcus, 15 to 20 gr of sulfanilamide, six times a day, with equal doses of sodium bicarbonate, has provided more than one therapeutic triumph.

#### INFECTIONS OF THE PROSTATE

Infections of the prostate should not enter into the discussion of infections of the kidney, but they are at times closely allied. Eight cases of prostatic abscess occurred in this series. In at least 4 cases the abscess served as a focus for the development of septicemia and renal infection. In all 6 of the cases in which culture was obtained, the organism grown was hemolytic *S. aureus*.

The seriousness of the condition is exemplified by the facts that 5 of the 8 patients died and that the fatal outcome was directly due to the infection. Here is additional evidence of the susceptibility of the diabetic patient to staphylococci. It also emphasizes a site of origin that can be easily overlooked, this possibility has been pointed out for the nondiabetic patient as well (Kickham and Welch<sup>12</sup>).

#### SUMMARY

A study is presented of 86 cases of renal infection in diabetic patients in the last five years at the George F. Baker Clinic, of which 37 were fatal, with 31 autopsies.

Diabetic cases in varying degrees present unique factors predisposing to infection of the urinary tract.

Infections of the urinary tract are more frequent, more protracted and more serious in outcome in the diabetic patient than in the non-diabetic.

A decrease in the incidence of the hematogenous type of renal infection has occurred in the last five years, as compared with the pre insulin and early-insulin eras.

The mortality of hematogenous renal infections in diabetes is high, owing to the fact that such infections are caused almost exclusively by hemolytic *Staphylococcus aureus*. Through early recognition and surgery, much can be done to lower the mortality.

The interval between a purulent infection of the skin and the onset of symptoms due to renal infection may be deceptively long, warranting periodic check-ups.

The colon bacillus is the most frequent pathogenic organism for both pyelitis and the parenchymal ascending type of infection. The streptococcus in any form has been rare.

Catheterization of diabetic patients should be employed only as an absolute necessity.

In the absence of mechanical obstruction, ammonium mandelate for the colon bacillus and sulfanilamide for streptococci have proved very successful therapeutic agents. No drug has yet given favorable results in kidney infections due to hemolytic *S. aureus*.

Prostatic abscess is a genitourinary focus of infection easily overlooked, and highly fatal to diabetic patients, usually through septicemia and renal infection.

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## REPORT ON MEDICAL PROGRESS

### RADIATION THERAPY

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#### TECHNICAL CONSIDERATIONS

EXPERIMENTS have been carried on at the Massachusetts Institute of Technology by members of the high-voltage research group, using cathode rays (electrons emanating from a hot filament in a vacuum) accelerated by potentials as high as 1,500,000 volts<sup>1</sup> It has been found that a penetration of about 7 mm in human tissue can thus be obtained This range is sufficient for exploring some of the physiologic effects of cathode rays, and may later prove of medical interest in the treatment of superficial malignant conditions Cathode rays are believed to have the advantage of producing less skin damage than do roentgen rays, and of delivering higher intensities at the inner portion of a neoplasm It is expected that in the future substantial increases in voltage will be made so that the penetration of cathode rays can be gradually extended to more deep-seated malignant tumors The generator<sup>2</sup> used in this research is adaptable to the production of x-rays and is now in routine operation at the Massachusetts General Hospital

Merritt<sup>3</sup> describes a technic for the x-ray treatment of new growths within the mouth and of the uterine cervix by means of specially designed intra-oral and intra-vaginal cones Twenty-five cases of intra-oral carcinoma have been treated to date, 16 of which have been followed for twelve to twenty months Of these 50 per cent have shown no local recurrence

Avoiding any controversy as to the relative value of high-voltage and low-voltage therapy, Carty and Ray<sup>4</sup> report their experiences with low-voltage, high-intensity x-radiation in experimental animals and in 12 patients suffering from brain and cord tumors This type of treatment is so new that no conclusions as to its ultimate value can be drawn It seems, however, to offer some promise This therapeutic method has become

available through the great advancement that commercial x-ray concerns have made in the construction of flexible, shock-proof radiotherapeutic apparatus

#### TREATMENT OF MALIGNANT CONDITIONS

A most comprehensive and encouraging publication on the treatment of carcinoma of the uterine cervix has been made by Smith and Pemberton<sup>5</sup> These authors report on 780 case with indisputable pathological confirmation of the disease The best percentage of five-year survivors among unselected cases (42 per cent) was achieved by the administration of radium plus supplementary x-radiation The adjuvant effect of x-radiation becomes even more apparent in those patients who received at least 3200 r 47 per cent were alive at five years It is noted that with heavy external roentgen radiation there is a greater percentage of complications than occurs when radium alone is used No significant difference in behavior or response to therapy can be discerned between adenocarcinoma and squamous cell carcinoma Clinical classification and pathological grouping are omitted as practically useless in the evaluation of therapy It is observed that with the proved results from the use of x-ray and radium in the treatment of carcinoma of the cervix, the indications for surgery are becoming very much restricted

Fricke and Bowing<sup>6</sup> point out that in cases of carcinoma of the cervical stump careful irradiation can accomplish much and that the prognosis is not hopeless However, much remains to be accomplished in the way of prevention The seriousness of carcinoma of the surgical stump must be publicized and re-emphasized Whenever subtotal hysterectomy is performed a conscientious examination of the cervix should be a requisite After such an operation the patient should have pelvic examinations at stated intervals, and should

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be instructed to come to the surgeon voluntarily for attention if vaginal bleeding occurs.

The x-ray treatment of 14 cases of primary in operable carcinoma of the bladder is reported by Pfahler.<sup>7</sup> When the tumor does not regress completely from the effects of external treatment, fulguration by the cystoscopist is recommended. Fifty per cent of these cases have been free of disease from two to nine years.

Payne<sup>8</sup> reports on malignant tumors of the testicle. He advocates that treatment be started early, and prefers a combination of radiation and surgery. The Aschheim-Zondek test is recommended in doubtful cases, and should be used to detect recurrences and to follow the response to radiation therapy.

Ninety-four cases of lymphosarcoma of the stomach have been added to the literature by Archer and Cooper.<sup>9</sup> Thirteen five-year cures in the series have been disclosed, 8 accomplished by irradiation, 1 by surgery and 4 by a combination of surgery and radiation. The authors believe that surgery is of limited value and should be confined to sharply defined small lesions.

It is generally agreed that surgery is the method of choice in the treatment of carcinoma of the colon, and that radiation should be reserved for those cases which are inoperable or recurrent after operation. Treatment with 200-kilovolt roentgen rays has given such discouraging results that it has been largely discontinued. X-rays produced at higher voltages seem to afford better palliation, and large doses are tolerated with less general reaction on the part of the patient. Relief from pain, diminution of bleeding and regression in the size of the growth have been observed.<sup>10</sup>

Meland<sup>11</sup> believes that radiation is preferable to surgery in carcinoma of the anus. This lesion almost always belongs to the epithelioma group and histologically it is the type that responds readily to x-ray or radium or a combination of the two. The curability ranks on a par with surgery and the morbidity is low. The physiologic sphincter control is retained except where the sphincter is already partly destroyed by disease.

In considering preoperative and postoperative x-ray treatment of carcinoma of the breast Pendergrass and Hodes<sup>12</sup> express some doubt as to the efficacy of this method as a routine procedure. Schmitz, however, in discussing this paper draws a comparison between 75 cases which were treated with surgery alone, and 75 treated by radical mastectomy plus radiation. At the end of five years the percentage of survivors from surgery alone was 18 per cent. The five-year survival of those patients who received radiation in

addition to surgery was 37 per cent. Schmitz points out that the radiation dose which he employed was considerably larger than that used by Pendergrass and Hodes.

Taylor and Meltzer<sup>13</sup> report on inflammatory carcinoma of the breast. This type of lesion occurs in 4 per cent of breast neoplasms. The condition is to be distinguished from true inflammation, radiation dermatitis, Paget's disease, adenocarcinoma, lymphoma, chemical irritations and so forth. A differential diagnosis is often exceedingly difficult. Treatment of these cases has not been satisfactory. Surgery has been followed by early metastasis to the supraclavicular nodes, skin recurrences and invasion of the remaining breast. Irradiation may produce early spectacular improvement, but unfortunately this does not last.

Craver<sup>14</sup> believes that aspiration biopsy is essential for the earlier diagnosis of a large proportion of cases of carcinoma of the lung, and that treatment of this disease by high-voltage roentgen irradiation can accomplish a great deal in a palliative way. With improvement in roentgen technique, better results may be anticipated in a disease which in the great majority of cases is not suitable for surgical intervention.

Mallet<sup>15</sup> has treated over 600 cases of widely disseminated malignancy by exceedingly small daily doses of x-ray given at a long distance. Although statistical data cannot be offered to show that many of these patients have been cured, it is nevertheless definitely stated that in most cases life was prolonged and symptoms ameliorated.

In a brief review covering the use of superhard x-rays in the treatment of cancer, Mudd<sup>16</sup> enumerates its advantages over 200-kilovolt treatment as follows: increase of skin tolerance, based on the dosage measured with a standard air chamber; greater penetration of the beam itself, providing intrinsically a greater depth dose at 10 cm; relative independence of depth dose and of portal dimensions, thus permitting the selection of multiple therapeutic fields of just sufficient size to include the volume to be irradiated (the skin area in this way can be used to greater advantage in planning treatment, and irradiation of tissues and organs adjacent to the tumor minimized); the more uniform distribution of radiation at 10 cm depth; and the existence, suggested by some workers, of a biological advantage due to wave length. Mudd sees little value in employing this type of radiation for superficially located malignancies but indicates that it is advantageous in the treatment of deep-seated lesions. These observations are in accord with those I<sup>17</sup> have recently published.

## TREATMENT OF NON-MALIGNANT CONDITIONS

There is an ever-growing interest in the use of x-rays and radium in the therapy of nonmalignant tumors, infections and endocrine disorders

In the treatment of angiomas in children, Paterson and Tod<sup>18</sup> evaluate three methods: surgical excision, cauterization and irradiation. When the lesion is small and there is plenty of tissue available to close the incision with tension, a small linear scar results from surgery and a safe and permanent cure is obtained. Cauterization by carbon dioxide snow, electrolysis or diathermy may be used for small lesions, but for large lesions the white scarring produced is unsightly. Irradiation either with gamma rays of radium or with well-filtered roentgen rays is the method of choice in all but capillary angiomas. A high percentage of cures results, and if the radiation is properly carried out a good cosmetic result without risk of damage to the skin may be expected.

The results of radium treatment in 34 cases of fibrous plaque of the penis are reported by Fricke and Olds<sup>19</sup>. In the earlier stages of the condition the prognosis following this type of therapy is good, in the later stages, that is, when the condition has been present for more than two years, treatment should not be urged.

Irradiation is finding a progressively wider range of usefulness in the treatment of paranasal sinus infections. Firor and Waters<sup>20</sup> have obtained good results with dosages which are well within the limits of safety.

It is claimed by Brown, Titche and Lawson<sup>21</sup> that x-ray treatment of acute catarrhal otitis media results in prompt relief from pain and a return of the drum membrane to normal in two or three days. In cases of acute purulent otitis media, the pain is relieved in a few hours, but the most useful effect of roentgen therapy is that exerted on the discharge, which instead of continuing for four to six weeks following myringotomy or perforation clears up in about a week. Good results are also reported in cases of chronic purulent otitis media.

Retropharyngeal swelling in children is readily demonstrable by x-ray examination and is usually due to some focal infection in the upper-respiratory tract, often the nasal accessory sinus. If both the focal infection and the retropharyngeal swelling are treated promptly with roentgen rays, a retropharyngeal abscess rarely develops.<sup>22</sup>

It is now fairly well established that the etiologic agent in lymphogranuloma venereum is a filterable virus. The first manifestation of the disease is usually a small ulceration or multiple herpetic-like vesicles on the genitalia. The disease is prone

to extend to the regional lymphatic nodes, but most patients have no systemic complaints. However, in some cases there is an elevation of temperature with chills and sweats. Manifestations may occur in the mouth or pharynx as well as on the genitalia. Cicatricial changes and the formation of fistulas frequently develop. The lesions are essentially concerned with the lymphatics and are susceptible to x-ray therapy. The initial doses must be small, with protraction over a period of one to three months.<sup>23</sup>

Pierson and Smith<sup>24</sup> confirm the observation of several other authors that x-ray treatment of the entire body at long distance is the most effective method developed to date for producing prolonged remissions in polycythemia vera.

Kaplan<sup>25</sup> reports on a large group of functional gynecologic conditions. Small doses of x-ray have proved a valuable therapeutic agent in amenorrhea and the relief of sterility. If radiation is properly given there is no harmful effect on the mother or the offspring. Rock et al<sup>26</sup> report similar results.

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 26331

### PRESENTATION OF CASE\*

*First Admission* A thirteen month-old boy entered the hospital for the first time because of vomiting of eleven months' duration, and failure to gain weight.

He was born at term after a labor lasting three hours and appeared normal at birth, weighing 6 pounds, 5 ounces. He was started on breast feedings and regained his birth weight in ten days. He never nursed vigorously, however. From an early age he was given a variety of feedings, any of which would be adequate under ordinary circumstances. The many changes were dependent on the fact that he failed to do well. Accessory vitamins had been given in adequate amounts since the age of three months. From the age of two months he vomited after almost every meal. Vomiting was usually projectile and usually occurred immediately after meals. Rarely would he go through a day without vomiting. The vomitus never contained blood or bile. Thick food seemed to be followed by vomiting more often than was liquid food. Beginning at two months it was noted by the parents that the stools were light yellow and frothy and appeared to be greasy, they also contained moderate amounts of undigested food particles. His weight gain all along had been poor: one month 7 pounds, 8 ounces; four months 11 pounds, six months 11 pounds, 6 ounces; ten months 12 pounds, 2 ounces; twelve months 12 pounds, 12 ounces. An additional prominent feature of his illness had been a harsh unproductive cough, almost paroxysmal in nature, which had begun at the age of three months.

There were no siblings. Three and a half years previously there had been one stillbirth, there had been no miscarriages. Both parents were living and well. During the mother's pregnancy she had had no adequate diet.

Physical examination showed an emaciated infant, apathetic and listless, whose skin was pale and had very poor elasticity. Palpable lymph nodes were noted in many regions of the body, these were non tender and the size of small peas. The respirations were rapid and dyspneic, with

considerable retraction of the interspaces. The breath sounds were harsh, and resonance was normal, no rales were heard. The abdomen was flat, with visible peristalsis, there was no spasm or tenderness. The liver edge was two fingerbreadths below the costal margin. No other masses were palpated.

Examination of the urine showed a trace of acetone. The blood showed a red-cell count of 4,010,000 with 70 per cent hemoglobin, and a white-cell count of 20,900. A blood Hinton test was negative. Tuberculin tests with dilutions of 1:1000, 1:100 and 1:10 were negative. The serum calcium was 9.9 mg per 100 cc., the phosphorus 5.0 mg., the phosphatase 8.6 units, the cholesterol 58 mg., the sugar 100 mg., the protein 7.0 gm., and the nonprotein nitrogen 33 mg. The blood vitamin C was 0.8 mg per 100 cc., the vitamin A 8.7 units (normal) and the carotenoids 7.7 units (reduced). A glucose-tolerance test showed a rise of the blood sugar level from 95 to 122 mg per 100 cc. in a half hour, and a fall back to 92 mg at the end of one hour. A vitamin A tolerance test showed fasting 8.7 units per 100 cc., nine hours 6.8 units, twelve hours 4.0 units and twenty four hours 7.9 units, these values remained unchanged when material was given by duodenum and when Mechoyl<sup>1</sup> was given. The stools were bulky, foul smelling and gray, and gave a negative test for blood. A three-day stool analysis showed a total weight of 683 gm., a total fat of 24 per cent and a total nitrogen of 1.6 gm. Analysis of the duodenal enzymes showed no steapsin, no amylase and 2.31 units of lipase, the normal values being 40 to 60, 50 to 100 and 15 to 30 units respectively. The sedimentation rate was within normal limits.

X-ray films of the chest showed considerable peribronchial thickening and infiltration. A barium enema was given and showed no abnormality, the cecum was moderately mobile, but remained in the right lower quadrant. A gastrointestinal series showed considerable irregularity in distribution, and clumping of the barium in the small intestine, the stomach emptied slowly.

He remained in the hospital for five and a half months, during which time efforts were made to improve nutrition without success. He developed definite otitis, and a myringotomy was performed. About two months after admission adenoidectomy was done to control the infection in the ears. He had a severe cough from the time he was admitted, and associated with this, rales could be heard diffusely throughout the lungs. His weight fell from 12 pounds, 3 ounces, on admission to a low point of 10 pounds three months later, but was 11 pounds, 7 ounces, at the time

\*This case is presented through the courtesy of the Children's Hospital, Boston.

of discharge. It was thought that his disease had been thoroughly studied in the hospital during this time, and owing to the anxiety of his parents, he was transferred home. His discharge diet included pancreatic enzymes.

*Final Admission* (two weeks later) He remained at home for two weeks, during which time his mother kept a daily weight chart. This showed a rise to 11 pounds, 15 ounces, and then two days before the second admission a sudden jump to 12 pounds, 8 ounces, and on the following day an increase to 13 pounds, 4 ounces. He came to the Out Patient Department for a routine follow-up visit on that day and was seen to be in obvious cardiac decompensation, with marked edema, pallor, coldness of the extremities and cyanosis. He was admitted, placed in an oxygen tent and rapidly recovered from the immediate decompensation so that he could be taken out of oxygen. There was a steady loss in weight from 13 pounds, 6 ounces, to 10 pounds, 14 ounces. The temperature fluctuated during this admission, rising on the day before death to 104°F. There was a gradual downhill trend, and he died approximately two weeks after the second admission.

#### DIFFERENTIAL DIAGNOSIS

DR. RALPH W. DAFFINEE. Here is the case of a baby who did very well in the neonatal period, but who did not gain in spite of numerous formula changes through the later part of the year. The vomiting was projectile and usually occurred immediately after meals, facts which make us think of pyloric obstruction. However, thick food seemed to cause more vomiting than did thin food, a finding which is not typical of congenital hypertrophic pyloric stenosis. At two months the stools began to show abnormalities. They were light yellow, frothy and greasy, all of which mean that his food was not being digested, particularly the fats. I do not believe we can say much about the chronic cough. Coughs at this age are usually due to chronic infection of the lungs or to congenital heart disease with secondary pulmonary changes.

We wonder whether the face showed the same changes as did the body. In chronic intestinal indigestion it is remarkable how often the face appears fairly normal, not until you have taken the clothes off the baby do you notice how terribly emaciated the trunk and extremities are.

He had palpable lymph nodes. There must have been some sort of infection. I do not know why the respirations were rapid and labored in the absence of significant lung signs. There is no description of the cardiac findings. One wonders whether there may have been some congenital

cardiac abnormality which was producing secondary pulmonary obstruction. Visible peristalsis can often be seen even in well infants when the abdominal wall is very thin, and I do not attach much clinical significance to this. The liver edge should not be palpable in so emaciated an infant. The liver is a fairly good index of nutrition, and in a well-nourished baby the liver edge comes down where it can be easily palpated. Congenital syphilis will produce a large liver in a very malnourished baby.

From the clinical standpoint I do not believe we are helped a great deal by most of the exhaustive laboratory work. There are numerous important points, however. The blood count was 4,000,000, with a low hemoglobin, and there was a certain degree of dehydration along with the acidosis that was evidenced by the acetone in the urine. The chemical constituents of the blood were essentially normal until we get to the cholesterol level, which in children is rather lower than it is in adults—normal values range from 126 to 280 mg per 100 cc. The vitamin contents seem to be normal except for that of the carotenoids, and I am not sure what that reduction means. The glucose-tolerance test showed a rise in the blood-sugar level from 95 to 122 mg per 100 cc, in other words the rise was not so high as we should expect. There was then a fall back to 92 mg, the typical flattened curve that we see in chronic intestinal indigestion. The vitamin A tolerance I cannot interpret, it seems to me the curve was upside down. The stool showed a total fat of 24 per cent, which is increased, but not so much as we often find it in celiac disease. I should like to know about free fatty acids. This was formerly considered a good differential diagnostic point between pancreatic insufficiency and celiac disease. The absence of duodenal enzymes is a most important finding, and to me it points directly at a lesion in the pancreas.

There are two additional points I should like to know about the x-ray: whether there was any evidence of osteoporosis, and the appearance of the heart.

DR. JOHN F. MCCREARY\*. I think a moderate degree of osteoporosis is quite evident in these films. So far as the heart is concerned there is little evidence of enlargement or any other abnormality.

DR. DAFFINEE. Is the peribronchial thickening typical of pneumonia?

DR. MCCREARY. No.

DR. DAFFINEE. From the time of his first admission the patient showed signs of inability to deal with infection. The chronic malnutrition be

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came steadily worse. The rapid rise in weight before the second admission must mean edema. The fundamental condition seems to have been either celiac disease or a cystic fibrosis of the pancreas. Celiac disease is a symptom complex rather than a definite disease. It is characterized by an arrest in growth, by a distended abdomen and by diarrhea with copious, pale, foul-smelling stools. With recent work, particularly on the pancreas, we have been able to eliminate some of the cases of so-called "celiac disease" and classify them under a separate heading. Our old criteria were the presence of fatty acids in the stools, and whether or not there was a response to the celiac diet. I was taught that if there was response to a celiac diet the condition was celiac disease, if there was no response it probably was pancreatic fibrosis. That has been disproved within the last few years. It seems to me that we are left with the diagnosis of a cystic fibrosis of the pancreas, associated with a lack of vitamin A. I interpret the findings in the lungs to be those of chronic vitamin A deficiency, with the laying down of keratin all over the bronchi, and terminally, bronchopneumonia. Dr. Farber probably will be able to tell us more about which came first in the pancreas, vitamin A deficiency with the laying down of plugs in the ducts, or a pancreatic lesion producing the vitamin A deficiency. I think that probably there was something wrong with the heart. The decomposition on the second admission I should interpret as being due to cardiac failure.

DR. TRACY B. MALLORY: The question of vitamin A deficiency has been raised here, and Dr. Farber has very thoughtfully brought along Dr. McCreary, who is particularly interested in this field. I wonder if he would discuss it a little for us.

DR. MCCREARY: As your abstract says, this child had a vitamin A tolerance test in which the levels for vitamin A in the samples taken after the fasting specimen were lower than that of the fasting specimen itself. In normal individuals we have found that the test shows a rise averaging 122 units above the fasting level, and this occurs somewhere between three and ten hours after the test dose of vitamin A is given. As a test dose we give 0.1 cc. of oleum percomorphum per pound of weight. Thus, this baby who had a fasting level of 87 units, somewhere between five and ten hours later should have had a level of 130 units, if he had been a normal child. Obviously there is a definite abnormality. We found in doing a series of vitamin A absorption tests that one condition in which there is a poor rise is cystic fibrosis of the pancreas. In celiac

disease we also get a poor response, sometimes of 10 units, sometimes as high as 20 units, but in no other condition do we find as poor a rise as in cystic fibrosis of the pancreas. To remark on the fasting vitamin A level, 8.7 units per 100 cc. is a normal level for this age and would make one think this child had received large doses of vitamin A in the form of some concentrate, in addition to the diet. Probably the carotenoid level, which was distinctly below normal, the average being somewhere between 15 and 20 units per 100 cc., represents his inability to metabolize fat. It simply means he was getting the carotenoids only in the diet but vitamin A was obtained from concentrates as well as diet. This is borne out when we inspect the history and find that he was getting 20 drops of oleum percomorphum daily.

These x-ray films show a slight degree of clumping here in the small intestines, and if this were observed under the fluoroscope, it would be seen that the clumps are singularly inactive. Little of the segmental peristalsis normally seen is apparent in children with celiac disease and pancreatic fibrosis.

#### CLINICAL DIAGNOSES

Pancreatic fibrosis  
Chronic bronchopneumonia

#### DR. DAFFINER'S DIAGNOSES

Cystic fibrosis of pancreas.  
Vitamin A deficiency  
Bronchopneumonia  
Congenital heart disease?

#### ANATOMICAL DIAGNOSES

Pancreatic fibrosis  
Chronic bronchopneumonia  
Bacteremia (*Streptococcus hemolyticus*)

#### PATHOLOGICAL DISCUSSION

DR. SIDNEY FARBER: \* I think that if Dr. Daffiner had discussed this case three years ago, he would not have been able to go as far as he went today and certainly would not have used the term "cystic fibrosis of the pancreas," a phrase coined only recently by pathologists.

I shall select from the many findings at autopsy the three most important ones. First there was a bacteremia, and the organism was *Streptococcus hemolyticus* which was grown from the heart's blood and from the lungs in pure culture. The second important finding was an acute and chronic bronchopneumonia. This type of pneumonia is

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found most frequently in seriously debilitated infants and children. It is the chronic interstitial type of pneumonia which begins with an interstitial involvement of the alveolar walls and peribronchial regions, bronchiolectasis and bronchiectasis finally occur. The dilated bronchioles and bronchi become filled with purulent material, caused either by the streptococcus or by secondary invaders such as staphylococci, and finally emphysema, atelectasis and widespread fibrosis of the lung complicate the picture. The third change was found in the pancreas. On gross examination the pancreas was narrower, much firmer in consistence and more pinkish red than is normal for a pancreas of a child of this age. These changes in the gross are so definite that they may be detected by the examiner's fingers, and the microscopic picture may be prophesied.

On microscopic examination the acini and small ducts are dilated and filled with material that is inspissated pancreatic secretion. Frequently the material is laminated or forms dense plugs. This change has nothing to do with vitamin A deficiency. A large part of the pancreas may be replaced by dilatation of the acini and ducts. Accompanying this change is atrophy of acini, and later replacement by fibrous tissue, so that the organ is greatly increased in consistence. Interestingly enough the islet tissue is not disturbed in any important or demonstrable manner. Dr S Burt Wolbach was the first to describe this picture, many years ago. We have seen it at autopsies now in well over 40 cases in advanced form, and in over 300 cases in minor degrees, so that we are able to trace the change from the very early to the advanced form, which we see here. Dr Wolbach gave an explanation which we have been able to verify as the material has accumulated. He postulated that the first change is alteration in the physical character of the secretion within the acini, that material inspissates and causes obstruction. Everything else that we see in the pancreas, he believed, depends entirely on the initial change in the character of the pancreatic secretion. We have found this change in the pancreas in every patient that has come to autopsy in our experience with such clinical diagnoses as celioid disease, chronic intestinal indigestion, pancreatic fibrosis and any other name which appeals at the moment. I think that is an important statement to dwell on for a moment, because of the differential diagnosis which Dr Daffinee made. Patients with true celiac disease, so far as I know, have not been studied at autopsy at the Children's Hospital. In true celiac disease it is believed that the pancreatic enzymes

are normal, in the condition under discussion today, pancreatic fibrosis or celioid disease, the pancreatic enzymes are deficient, as would be expected with such marked obstruction in the acinar system and fibrosis of the pancreas. The suggestion I want to make is that in celioid disease, if I may use that term, or pancreatic fibrosis, the pancreas plays an extremely important role in the pathogenesis of the disease and in the explanation of many of the disease symptoms.

Vitamin A deficiency was mentioned in discussion quite correctly by Dr Daffinee. It is interesting that the first time a patient was recognized as having died of vitamin A deficiency, — by Dr Wolbach in 1923, — the patient had vitamin A deficiency, pancreatic fibrosis and, in addition, one other unrelated condition, inclusion bodies in the submaxillary glands. We know that the first two conditions are not related except in the following fashion. If a patient does have pancreatic disease and if vitamin A is not added to the diet, or otherwise, in larger amounts than are normally required, then evidence of vitamin A deficiency will be present at autopsy.

There is an inconstant correlation between the chronic bronchopneumonia and pancreatic fibrosis. This type of chronic pneumonia does occur in patients who have no evidence of pancreatic disease. The only connection there can be between the pneumonia and the pancreatic changes is that changes similar to those in the acini do take place in the glands of the trachea and bronchi. Such changes may form the starting point for subsequent invasion by the hemolytic streptococcus.

## CASE 26332

### PRESENTATION OF CASE

A forty-three-year-old American barber entered the hospital complaining of swelling of the right testis.

Twelve years prior to entry the patient had noted the gradual enlargement of the left side of his scrotum. There was no pain, and during the ensuing three years he consulted several physicians who prescribed various ineffectual remedies. At the end of this period he entered another hospital, where a left orchidectomy was performed. An x-ray film of the chest taken preoperatively showed no evidence of metastases. The testis was found to contain "an undifferentiated carcinoma (embryoma)." Postoperatively several prophylactic roentgen treatments were given to the operative site. About one week after the operation he developed a phlebitis of the right leg, which subsided without complication. During the three succeeding

years the patient remained well. Six years before admission to this hospital he observed progressive painless enlargement of the right testis. During the last one and a half years the enlargement was somewhat more rapid, and for six months the testis was quite painful.

Physical examination showed a well-developed and well-nourished man without evidence of acute distress or weight loss. Examination of the heart, lungs and abdomen was negative. The blood pressure was 110 systolic, 70 diastolic. There was a healed surgical scar in the left scrotum, and the testis on this side was absent. The right testis was enlarged to almost 15 cm in diameter and was roughly spherical in configuration. The consistency was firm and rubbery, although there were several areas which were softer than others, and focal tenderness was elicited. The lesion did not transilluminate. No inguinal lymph nodes were palpated.

The temperature, pulse and respirations were normal.

Examination of the urine was negative. The blood showed a red-cell count of 5,900,000 with 90 per cent hemoglobin. The white cells numbered 9100, with 78 per cent polymorphonuclears. A blood Hinton test was negative. A urine culture was negative. A quantitative assay of the patient's urine for "teratoma" hormone was positive to a strength of 8 mouse units per liter. Further dilutions were not done.

An intravenous pyelogram and a plain abdominal film were negative. An x-ray of the chest showed no evidence of metastatic disease.

On the fourth hospital day an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

Dr. RICHARD CHUTE. Here is a middle aged man whose right testis, over the course of six years, has gradually enlarged to a firm, rubbery mass, larger than a grapefruit. There is an old history of embryoma of the other testis, which is, as you know, one of the relatively benign testicular tumors. I cannot see anything about the physical examination other than the local examination of the testis, which helps to make a diagnosis, except that the patient is not cachectic and there are no enlarged lymph nodes or spleen to suggest lymphoma.

In the laboratory findings it is stated that he has 5,900,000 red blood cells. This may be a laboratory error, but whatever its significance, I do not believe that it is important in arriving at the diagnosis. It is of great interest that he shows gonadotropic hormone in the urine. We do not

know exactly how much, because the preliminary assay done for this in the laboratory is for 8 mouse units, which in this case was positive. When doing a more thorough quantitative assay, the laboratory would test to see if the urine were positive for 40 or 100 units, but that was not done and all we know is that the patient has some gonadotropic hormone in the urine. We can guess, however, that he has not a great deal of this hormone because he apparently does not have gynecomastia, and individuals who excrete large amounts of gonadotropic hormone usually do have gynecomastia.

So far we have a man apparently in excellent general health who has had an embryoma of one testis, and now the hormonal study suggests that he may have another testicular tumor of embryonal tissue. In the differential diagnosis we have to consider hydrocele and spermatocele, which would give the same picture of a slowly growing mass in the scrotum and would not undermine a man's general health as long standing malignancy might. On the other hand, hydrocele or spermatocele usually transilluminates with light, and this does not. However, hydroceles with chronically thickened, fibrotic sacs do not transilluminate. Nevertheless, they usually do not have a hard, rubbery, firm consistency, and I should think that either hydrocele or spermatocele was not probable in this case. Scrotal hernia has also to be considered in the differential diagnosis, but the physical examination seems to rule that out.

Elephantiasis, which is a disease of the scrotum itself rather than of the testis, I think is out. There is nothing to suggest tuberculosis. He has a negative blood Hinton test, and therefore I presume it is not a gumma. Occasionally one sees metastases to the testis from somewhere else, for example in lymphoma, but there is nothing about this picture to suggest that. Therefore, the physical examination makes me think that neoplasm of the testis is still the most probable diagnosis. Although bilateral neoplasms of the testis are rare, they do occur. Therefore I am going to make a diagnosis of testicular tumor.

If he has a tumor which has been growing slowly for six years, it seems as if it cannot be a very malignant one. There is no evidence of metastases in the chest and no cachexia. In the presence of these distinguished pathologists I am a little timorous about discussing the classification of testicular tumors, which is a confusing subject and one about which even pathologists are not in agreement. However in a broad way there are two general groups of tumors. The first group



is that composed of the homologous tumors, which are formed by cells derived from the testis, and among which are a few fairly benign tumors, such as adenoma, and a good many malignant tumors, such as seminoma. The second and larger group is formed by the heterologous, mixed tumors, of which there are a few benign ones, such as dermoid cyst and congenital embryoma, and a great many which are extremely malignant such as malignant teratoma, embryonal carcinoma and so forth. Only embryonal tissue produces gonadotropic hormone, so that means that if this man has a testicular tumor he must have an embryonal one. It would appear that he has a relatively benign one on account of the fact that he apparently has not a great deal of the hormone, and because the tumor has been slowly growing for six years without having markedly depressed his physical condition. Therefore, I should say that he has a relatively benign variety of embryonal tumor, and since he had a congenital embryoma once before, I should make my guess that he has another now.

DR FLETCHER H COLBY So far as I know we have had two bilateral tumors of the testicle here, one was a lymphosarcoma, metastatic from a primary lesion in the nasopharynx, which was radiated and disappeared, and the other an embryonal tumor somewhat similar to this.

#### CLINICAL DIAGNOSIS

Embryonal carcinoma

#### DR CHUTE'S DIAGNOSIS

Neoplasm of testis (embryoma)

#### ANATOMICAL DIAGNOSIS

Carcinoma (? teratoma) of testis

#### PATHOLOGICAL DISCUSSION

DR. TRACY B MALLORY This patient was operated on and a large tumor resected. On section it was found to consist of two parts: one was a solid tumor mass, very necrotic, and the other a cyst of significant dimensions, about 6 cm in diameter. So I think it is quite possible that it was a cyst that he had for six years and that the tumor may have been of recent origin, because on microscopic examination the tumor is obviously a very highly malignant one and it does not seem possible that he could have had it for six years without generalized metastases and death. As to what the tumor is, I am not going to commit myself very far. It is a highly undifferentiated neoplasm with cells that vary a great deal in size and shape, with many multinucleated giant cells. It is not the ordinary seminoma or any of the other specific forms. There is nothing that permits me to make a diagnosis of teratoma, since only epithelial tissue is present. Only when one can find sarcomatous elements or chorio-epithelial elements can one positively make such a diagnosis. My guess is that this is a teratomatous tumor which is only differentiated in one direction—toward the epithelial side. However, I think one guess would be quite as good as another on that. All I am willing to say is that it is a highly malignant carcinoma.

A PHYSICIAN Was the cyst a dermoid?

DR MALLORY It was a simple cyst surrounded and invaded by tumor. We could not identify it. It may perfectly well have been a hydrocele.

DR. J H MEANS What is the outlook? Is it apt to recur?

DR. MALLORY He is almost certain to have recurrence.

# The New England Journal of Medicine

Formerly the  
Boston Medical and Surgical Journal  
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND  
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE  
ON PUBLICATIONS

Official Organ of

THE MASSACHUSETTS MEDICAL SOCIETY  
THE NEW HAMPSHIRE MEDICAL SOCIETY  
THE VERMONT STATE MEDICAL SOCIETY

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**SUBSCRIPTION TERMS:** \$6.00 per year in advance, postage paid, for the United States; Canada \$7.25, Boston (outside including war-exchange tax) per year; \$8.50 per year for all foreign countries (belonging to the Postal Union).

Materials for early publication should be received not later than noon on Saturday.

This journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the New England Journal of Medicine, 8 Fenway Boston, Massachusetts.

## MEDICAL PREPAREDNESS THE HEALTH OF THE NATION

The first prerequisite of a nation prepared to defend itself successfully is physical, mental, and moral health. As Surgeon General Thomas Parran\* has stated, "It is urgent now that the people of this nation be physically tough, mentally sound, and morally strong. And it is obvious that the conquests in Europe during the past eleven months have been consummated by a nation whose people are healthy, even though their moral standards, at least according to American ideas, are open to question."

National health is an extremely important problem even in times of peace, and much has been accomplished, particularly during the past twenty-five years, in its promotion. Little or nothing, however, has been done toward a health census of large groups of the population, the correction,

so far as possible, of the remediable faults that are found, and the nation-wide application of approved methods of preventive medicine.

The conception as to how all these could be achieved is difficult. As a beginning, Surgeon General Parran has suggested the appraisal of the 300,000 young people employed by the National Youth Administration and of the nearly 2,000,000 men and women enrolled under the Work Projects Administration, with a subsequent listing of those best qualified or, because of remediable defects, potentially qualified for industrial training. Selective, compulsory military training, with physical examination of those drafted into service, would furnish data on a certain group of young men but would neglect by far the majority of the population. Through group examination little would be gained toward the correction of the nutritional defects that are known to exist among a large proportion of the working class, and preventive medicine would receive scant consideration.

While it is true that all these problems have, for many years, been the concern of various federal agencies, public health departments of states, cities and towns, national foundations and other organizations interested in health and disease, and the associations and the individual members of the medical and allied professions, the work of each has been done independently. The present crisis demands intelligent co-operation, and the need for a medical co-ordinator, as suggested by Surgeon General Parran and by the Committee on Medical Preparedness of the American Medical Association, is probably more urgent in this aspect of medical preparedness than in any of the others. In fact, as has already been suggested in the *Journal*, it seems as though the conditioning of the nation were so important and so vast an undertaking that it deserves the entire attention of an extremely capable and well-qualified physician rather than that portion of time which one concerned with all the problems of medical preparedness could devote to it. The appointment of someone to assume this responsibility is essential not only as a war-time but also as a peace-time measure.

## ILLUSTRATIONS

THE question of how best to reproduce x-ray and other photographs, to which attention is called by a correspondent in this issue of the *Journal*, is one that has always bothered the editorial staff. Cuts that have significant detail must fulfill certain requirements. In the first place, the original film must be well taken; a reproduction, no matter how the plate is made or on what grade of paper it is printed, is never so good as the original. Second, the reduction must not be too great. Third, in making the half tone a fine screen must be used. And, fourth, in printing, the make-ready must be attended to with the greatest of care and a heavy grade of coated paper must be used.

All except the third requirement and the last part of the fourth can be controlled by the editorial staff of any journal; reproduction of poor photographs can be refused, reductions can be properly gauged, and careful make-readys can be required of the printer. The size of the screen used in making the half tones, however, is entirely dependent on the grade of paper, and the latter, in turn, is governed by how much a journal can afford to spend for its stock. Obviously, a quarterly journal that sells for two and a half dollars a copy, such as one of the *Journal's* British contemporaries, can use a superlative grade of coated paper, whereas a weekly periodical that costs only twelve cents a copy, such as the *Journal*, is necessarily limited to a medium grade of so-called "book paper." It might be added that the book paper now used is a considerable improvement over that used several years ago.

The extra expense incurred by the use of coated stock and by the inclusion of colored plates in the *Journal* during the last few years has, in each case, been borne by the authors. For this assistance the editorial staff is grateful, for it not only improves that particular issue but also shows that good reproductions can be had, provided the necessary requirements are met.

To use nothing but coated stock would impose an added annual expense of about seventy-five hundred dollars, or one and a half dollars for each member of the Massachusetts Medical So-

ciety, whereas to use forms of coated stock for sections of issues in which photographs appear would cost approximately twenty-five hundred dollars a year, or fifty cents for each member. With an increasing circulation it is hoped that the *Journal* will eventually be able to use coated paper without added cost to the Society, but at present, a request for an increase in the amount of money annually allotted to the *Journal* does not seem warranted.

## MEDICAL EPONYM

## CORRIGAN PULSE

Aortic regurgitation had been described by several physicians before the appearance of a communication by Dominic John Corrigan (1802-1880), physician to the Charitable Infirmary of Dublin and lecturer on the theory and practice of medicine at St. Patrick's College, Maynooth, in the *Edinburgh Medical and Surgical Journal* (37:225-245, 1832), "On Permanent Patency of the Mouth of the Aorta, or Inadequacy of the Aortic Valves," but his account has become a classic.

When a patient affected by the disease is stripped, the arterial trunks of the head, neck, and superior extremities immediately catch the eye by their singular pulsation. At each diastole the subclavian, carotid, temporal, brachial, and in some cases even the palmar arteries, are suddenly thrown from their bed, bounding up under the skin. Though a moment before unmarked, they are at each pulsation thrown out on the surface in the strongest relief.

R W B

## MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS  
AND GYNECOLOGY\*

RAYMOND S. TITUS, M.D., *Secretary*  
330 Dartmouth Street  
Boston

## INHALATION PNEUMONIA

Mrs. M. W., a thirty-four-year-old para III at term, was sent into the hospital in labor on November 22, 1924.

The family history was non-contributory. The past history included measles, sore throats and a light case of influenza during the epidemic. There

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

had been no operations. The two previous pregnancies had been uneventful and both had ended in instrumental deliveries. Catamenia began at thirteen, were regular with a twenty-eight-day cycle and lasted five days without pain. The last period began on February 24, making the expected date of confinement early in December.

The pregnancy had progressed normally and uneventfully. The patient was seen in the office on November 14, at which time the weight was 154 pounds, a gain of 35 pounds, the lungs were clear and resonant, the heart was not enlarged and was regular. The blood pressure was 126 systolic, 60 diastolic. The abdomen was enlarged to the size of a full-term pregnancy, with the fetal heart heard on the right.

Vaginal examination on admission to the hospital showed the cervix thin, taken up and dilated about three fingerbreadths. Labor progressed normally and rapidly. The patient was anesthetized with nitrous oxide, oxygen and ether anesthesia, which was taken poorly, and a simple forceps delivery was done. The baby was a boy weighing 7 pounds, 12 ounces, and was in good condition. On coming out of the ether, the patient became very blue, coughed a great deal and vomited a large quantity of undigested food. It is possible that she inhaled some of the vomitus.

For the next three days the patient ran an afternoon temperature of 101°F., with a pulse of 120 and respirations of 30. Consultation was held with an internist, who found dullness over the right back, with definite congestion at the angle of the scapula. This finding was confirmed by x-ray examination. Forty-eight hours later a second x-ray film showed that the lung was clearing. The temperature and pulse came slowly down to normal, and the patient was discharged in good condition on December 13.

*Comment.* Fortunately, this case of inhalation pneumonia was not severe, the febrile reaction lasting only five days, during which time the patient was not ill. The only time that her condition gave any apprehension was immediately following delivery, when coughing and vomiting occurred, she became very cyanotic and the pulse and respirations were very rapid. If one could always tell when labor was imminent, patients might be advised to abstain from solid food. One of the great advantages of elective induction is that labor is induced when the stomach is empty, thus avoiding any possible inhalation of vomitus when the patient comes out of the anesthetic.

## DEATHS

**FERRINI**—PETER FERRINI, M.D., of Middleboro, died August 5. He was in his forty-first year.

Dr. Ferrini received his degree from the Harvard Medical School in 1927 and at the time of his death was assistant superintendent of the Lakeville State Sanatorium, Middleboro.

He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son and a daughter survive him.

**ROGERS**—ALBERT E. ROGERS, M.D., of Boston died recently. He was in his seventy-fourth year.

Born in Charlestown he attended school there, later graduating from Harvard University. He received his degree from Harvard Medical School in 1890 and did postgraduate work at the University of Berlin and the University of Vienna.

He was a fellow of the Massachusetts Medical Society and the American Medical Association and was a member of the Boston Medical Library.

His widow and a son survive him.

**ST. CLAIR**—AUSTIN E. ST. CLAIR, M.D., of Framingham died August 7. He was in his seventy-sixth year.

Born in Tenant's Harbor, Maine, he received his degree from the University of Vermont College of Medicine in 1893. He later studied at the universities of Vienna and Berlin and started practicing in Framingham.

He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow and a daughter survive him.

## MISCELLANY

### BRONCHOSCOPY IN TUBERCULOSIS

Bronchoscopy is a relatively new means of investigation in the diagnosis of tuberculosis. It is especially valuable for discovering tuberculosis of the tracheobronchial tree, a condition which though described over a century ago, is still treated too casually. Two clinicians, associated with a sanatorium where bronchoscopy is a routine procedure, have pointed out its value and reported their experiences. An abstract of their article (Sharp, J. C. and Gorham, C. B. Routine Bronchoscopy in Tuberculosis. *Am Rev Tuberc* 41:708-718, 1940) follows.

Bronchoscopy is not contraindicated except in cases of acute laryngeal tuberculosis, recent extensive hemorrhage, far-advanced tuberculosis with toxemia and cachexia. Even these contraindications may be considered only relative in isolated cases. Bronchoscopy in the tuberculous is now an accepted procedure by many phthisiologists and bronchoscopists.

The indications for bronchoscopy have been listed as a diagnostic procedure for differential diagnosis as a diagnostic study in proved cases of tuberculosis with certain signs and symptoms to assist in carrying out endobronchial procedures, such as the instillation of opaque media or for therapeutic purposes.

#### *Tracheobronchial Tuberculosis*

There are apparently two methods of the development of tuberculous tracheobronchial lesions by continuity through direct extension from neighboring structures as through the lymphatics, and by the implantation of bacillary sputum on the mucosa. Several types of lesions have been observed, namely diffuse and nodular mucosal or

submucosal lesions, ulcerative lesions, fibrostenotic lesions and various combinations of these

A wide variation in incidence has been reported by various writers. One group of workers found tuberculous tracheobronchial lesions in 41 per cent of autopsies of tuberculous cases and another worker reports only 44 per cent tuberculous lesions in the major bronchi.

The development of the bronchoscope has stimulated the study of tuberculous tracheobronchitis in the living, not only from the diagnostic viewpoint, but also in relation to pulmonary disease, as well as with regard to the therapy of the local lesion.

The symptoms of tracheobronchial tuberculosis are wheezing or asthmatic attacks, paroxysmal attacks of intractable coughing with production of variable amounts of thick tenacious sputum at different intervals, dyspnea out of proportion to vital capacity with inspiratory stridor, cyanosis, constant clearing of the throat, persistently positive sputum in the absence of other evidence of pulmonary tuberculosis, and intermittent atelectasis. It is apparent, in view of the experience of many and the recent extensive literature, that these cases should be bronchoscoped before any major surgical procedure for diagnostic reasons, as well as for therapeutic relief. It is also true that bronchoscopy should only be considered as a supplemental part of the complete examination of the patient. It also should be stressed that bronchoscopy should only be done by trained hands. A thorough knowledge of the anatomy of the structures involved is essential. It should be unnecessary to emphasize again that gentleness is of extreme importance, and that psychic as well as physical trauma of the patient must be avoided.

#### *Authors' Experiences*

After describing the bronchoscopic appearance of lesions, treatment procedures and other considerations discussed by various writers, the authors offer their own experiences. For the past two years all patients admitted to the Monterey County Sanatorium have been routinely studied by bronchoscopy, unless definitely contraindicated. Criteria were rigid and the findings of one observer were checked by the other. In a series of 53 cases definite tuberculous tracheobronchitis was found in 37 per cent. Nearly all the lesions were early mucosal and submucosal ones, and most showed definite visible tubercle formation. The majority were on the posterolateral and posteromedial walls of the main bronchi on the side of the pulmonary lesion. In only 3 of 20 definite cases were there symptoms. All cases were treated by local applications of 30 per cent silver nitrate, and all but 1 patient have shown improvement on repeated examination and treatment, with apparent definite healing in 6. Healing has been interpreted by a flattened and normal appearing mucous membrane at the site of the previous lesion. In one other case a recurrence of the tracheobronchial ulceration occurred three months after there was apparently definite healing. Several cases with negative findings have been bronchoscoped, subsequent to collapse procedures, for check up on persistently positive sputum and no bronchial lesion was found.

There were no complications attributable to bronchoscopy and no apparent ill effects in over one hundred examinations. Patients accept bronchoscopy as a matter of routine. Carefully performed bronchoscopy is a relatively simple procedure which carries practically no risk, and yields a considerable amount of valuable information.

#### *Summary and Conclusions*

Tuberculous tracheobronchitis has an important bearing on the prognosis and treatment of pulmonary tuberculosis.

Advanced and progressive ulcerative or stenotic lesions are serious complications.

Little is known of the evolution of early lesions and this is extremely important if they become progressive.

Early lesions occur without the classic symptoms of obstructive lesions.

Bronchoscopy of the tuberculous, unless definitely contraindicated, is simple and practically harmless when performed carefully and gently by trained workers, and complications are rare.

Bronchoscopy is a routine procedure in many institutions before certain major surgical procedures and is becoming more so.

It is suggested that more bronchoscopic examinations be done on patients in sanatoriums, not only to enrich our knowledge of tracheobronchial tuberculosis, but also with the more important view of a more rational and better treatment of the patient.

There is no accepted method of treatment of tracheobronchial lesions, but 30 per cent silver nitrate locally applied seems to have some value, particularly in assisting in the healing of early lesions.—Reprinted from *Tuberculosis Abstracts* (August, 1940)

#### OSLER AT OLD BLOCKLEY

"Osler at Old Blockley," a painting in oil by Dean Cornwell, was unveiled at the dedication of the Osler Memorial Building on the grounds of the Philadelphia General Hospital this past June and was later exhibited at the meeting of the American Medical Association in New York.

The painting depicts one of Osler's outstanding contributions to medicine, namely, bringing medical students to the bedside of the patient for clinical study. In the painting Osler is shown at the side of an elderly patient on the hospital grounds. Surrounding Osler and the patient are interns who have stopped with him as they were on their way to the autopsy house to observe one of



his famous postmortems. This autopsy house, now the only Osler memorial building in the United States, is shown in the background. This memorial was made possible by a grant from John Wyeth and Brother.

"Osler at Old Blockley" is the second painting in the series "Pioneers of American Medicine" sponsored by John Wyeth and Brother as part of a project to highlight the contributions of Americans to the advancement of medicine. "Beaumont and St. Martin" was the first painting in the series.

Colored reproductions of "Osler at Old Blockley," approximately 16 by 19 inches in size and suitable for fram-

ing, may be obtained free by addressing requests to *New England Journal of Medicine* 8 Fenway, Boston

## CORRESPONDENCE

### ILLUSTRATIONS

To the Editor I congratulate the *Journal* for the relatively excellent reproductions of the x-ray photographs in Colby and Suby's article in the July 18 issue. I notice you have used a special glazed [coated] paper. May I as one of your young but faithful readers suggest that you continue to publish x-rays and other photographs of this technical superiority or even better ones. These can be used with particular value in the "Case Records of the Massachusetts General Hospital." For example, the whole point of Case 26241 was the x-ray film of the chest which showed radiation pneumonitis. I can assure you that I speak for a large group of young physicians and students when I state that such additions would be of great value.

Realizing that this involves added expense, I suggest that you state the expense of publishing such reproductions in the hope of obtaining an expression of opinion from other readers.

A. C. ENGLAND, JR., M.D.

Boston City Hospital  
Boston.

## NOTICES

### PENTUCKET ASSOCIATION OF PHYSICIANS

The list of speakers and their subjects that have been scheduled for the 1940-1941 meetings of the Pentucket Association of Physicians is as follows: September 12 "Hemolytic Streptococcus Infection," Dr. Chester S. Keefe; October 10 "Recent Advances in Orthopedic Surgery," Dr. James W. Sever; November 14 "The Management of Serious Infections of the Hands," Dr. Howard M. Clute; December 12, "Arthritic Joints," Dr. Robert J. Joplin; January 9 "Acute Appendicitis," Dr. Elliott C. Corder; February 13, subject to be announced, Dr. Cadis Phipps; March 13 "The Diagnosis and Outline of Treatment for Nerve and Tendon Injuries in the Hand," Dr. William E. Browne; April 10 subject to be announced, Dr. Samuel A. Levine; May 8, "Ovulation and Menstruation," Dr. John Rock.

The September 12 meeting will be held at the "Try Angle," Groveland, at 8.30 p.m.

### AMERICAN OCCUPATIONAL THERAPY ASSOCIATION

The American Occupational Therapy Association representing a membership of about 1800 therapists from this country and foreign territories, will convene in Boston September 16 to 20, in conjunction with the American Hospital Association. Headquarters for the former group will be at the Hotel Somerset, 400 Commonwealth Avenue.

The local committee has completed a program in which leading persons from the New England medical centers will participate. The opening session on the afternoon of September 16, will take place at the Harvard Medical School where Dr. Edward D. Churchill will read a paper on "Surgery of the Chest," followed by a clinical presentation on "Treatment of Hand Injuries," by Dr. Henry C. Marble.

Other high lights of the program include the following round-table discussions: "Occupational Therapy in Community Health" — leader Miss Helen King, supervisor of physiotherapy and occupational therapy, Visiting Nurse Association, Detroit, Michigan; "Correlating Occupational Therapy with Rehabilitation Agencies" — leader Mr. Terry Foster, research agent, Vocational Rehabilitation Division, U. S. Department of Education, Washington, D. C.; "Education as a Therapeutic Agent" — leader Mr. Edward M. Parrish, director of study and craft guild, Saranac Lake, New York; and "Behaviour Problems as Related to Occupational Therapy" — leader Dr. George E. Gardner, Massachusetts General Hospital and Judge Baker Foundation.

Scientific and educational exhibits will be housed with those of the American Hospital Association in Mechanics Hall. A special showing of motion pictures, dealing with phases of occupational therapy throughout the United States, is scheduled.

In addition to the main registration desk at Hotel Somerset, an information desk will be maintained at the Hotel Statler. Transportation between the two hotels for American Hospital Association members who wish to attend the meetings of the American Occupational Therapy Association will be arranged.

### U. S. CIVIL SERVICE EXAMINATIONS

Senior Medical Officer \$4600 a Year

Medical Officer \$3800 a Year

Associate Medical Officer \$3200 a Year

The U. S. Civil Service Commission has announced open competitive examinations to fill medical-officer positions in the U. S. Public Health Service and Food and Drug Administration, Federal Security Agency, Veterans Administration, Civil Aeronautics Authority, Department of Commerce and Indian Service, Department of the Interior. Applications must be filed with the U. S. Civil Service Commission, Washington, D. C., and will be rated as received until further notice.

Applicants must have been graduated with an M.D. degree from a recognized medical school and must have had professional experience in one of the following optional branches: aviation medicine, cancer research, cardiology, dermatology, eye, ear, nose and throat (singly or combined), general practice, industrial medicine, internal medicine and diagnosis, medical pharmacology, neuropsychiatry, pathology, bacteriology and roentgenology (singly or combined), public health, surgery, tuberculosis and urology. For some positions in the Veterans Administration applicants for associate medical officer paying \$3200 a year need not have had experience other than one year of Internship. Applicants for the associate grade must not have passed their fortieth birthday and for the other two grades they must not have passed their fifty-third birthday.

Full information regarding the examinations and the application forms may be obtained from the Secretary Board of U. S. Civil Service Examiners, at any first-class or second-class post office, or from the U. S. Civil Service Commission, Washington, D. C.

Pathologist (Medical) \$3800 a Year

Applications must be on file with the U. S. Civil Service Commission at Washington, D. C., not later than September 9.

Applicants must have completed a four-year college course with major study in biology or chemistry or must

have been graduated from a recognized medical school, and must have had appropriate experience in pathology, either human or animal

Further information regarding the examinations, the detailed requirements and the application forms may be obtained from the Secretary, Board of U S Civil Service Examiners at any first-class or second-class post office, or from the U S Civil Service Commission, Washington, D C

## SOCIETY MEETINGS AND CONFERENCES

SEPTEMBER 2-6—American Congress of Physical Therapy Page 862, issue of May 16

SEPTEMBER 12-MAY 8—Pentucket Association of Physicians Page 263

SEPTEMBER 16-20—American Occupational Therapy Association Page 263

OCTOBER 6-11—Annual meeting of the American Academy of Ophthalmology and Otolaryngology Page 81 issue of July 11

OCTOBER 8-11—American Public Health Association Page 655 issue of April 11

OCTOBER 11-12—Pan American Congress of Ophthalmology Page 898 issue of May 23

OCTOBER 14-25—1940 Graduate Fortnight of the New York Academy of Medicine. Page 938 issue of May 30

OCTOBER 21—American Board of Internal Medicine. Page 369 issue of February 29

JANUARY 4, 1941—American Board of Obstetrics and Gynecology Page 1064 issue of June 20

MARCH 8—American Board of Ophthalmology Page 201 issue of August 1

APRIL 21-25—American College of Physicians Page 1065 issue of June 20

## BOOK REVIEWS

*Diseases of the Gallbladder and Bile Ducts* By Waltman Walters, BS, MD, MS, ScD, and Albert M. Snell, BS, MD, MS 8°, cloth, 645 pp, with 342 illustrations Philadelphia W B Saunders Company, 1940 \$10.00

This book is an excellent treatise on the diagnosis and treatment of diseases of the gall bladder and biliary tract, and it represents the extensive experience of the authors and other contributors on the staff of the Mayo Clinic. It is essentially the analysis of a large number of cases diagnosed and treated in a large clinic, and should serve as an excellent reference book to any physician or surgeon interested in the treatment of diseases of the biliary tract.

The book is divided into five main sections. Part I covers briefly the anatomy and physiology of the gall bladder. The diseases of the gall bladder and biliary tract are discussed by one who is well qualified, and the descriptive matter is clear and definite. Part II describes very clearly the diagnostic methods utilized in determining the presence of cholecystic disease or of gallstones. A review of the symptoms and clinical findings in disease of the gall bladder is given in this section, together with a discussion of tumors, and of differential diagnosis in association with other diseases of the upper part of the abdomen. Part III is given over to a consideration of diseases of the bile ducts and includes a discussion of choledocholithiasis and strictures, tumors and extrinsic lesions of the common duct. Part IV is of especial interest to physicians and surgeons because the medical and surgical treatment is clearly and conservatively outlined. The indications for surgery are discussed, they follow the principles and theories well known to physicians and surgeons for a long time. The section on surgical technic is particularly descriptive, and clearly represents the technical procedures as carried out at the Mayo Clinic. Part V is, in the main, a summary of the routine measures usually employed in the care of the patient before and after operation on the biliary tract.

The book has abundant illustrations, which have been

well chosen, are readily interpreted and adequately demonstrate the various diagnostic and technical methods.

One is impressed with the conservative attitude taken toward indications for surgery and also with the handling of cases of acute cholecystitis. The reviewer agrees with the authors that early operation in cholecystitis gives the most satisfactory results and lowest mortality. It is also of interest to note the emphasis placed on the frequency of common-duct stone and the necessity for exposure and palpation of the common duct in all cases and for the exploration of the common duct in a large percentage of these cases. The authors and their collaborators are to be commended for their concise and clear-cut description of diseases of the gall bladder and biliary tract. This book is recommended for reference for the general practitioner and the surgeon alike.

*The Newer Nutrition in Pediatric Practice* By I Newton Kugelmass, BS, MA, MD, Ph D., ScD 8°, cloth, 1155 pp, with 183 illustrations Philadelphia J B Lippincott Company, 1940 \$10.00

The author of this book has undertaken a very large task in attempting to bring together in a single volume all the information bearing on nutrition in children. He has not adhered strictly to his text, as there is an extensive discussion of many conditions which bear only a tenuous relation to nutrition, as illustrated in the section on infectious diseases.

One cannot but be impressed with the extent of the field covered in this volume. It is unfortunate that in the text there is very little separation in statement between the material drawn from the work of other investigators and the first hand knowledge or opinion of the author. At the end of each chapter there is a selected bibliography, but no direct credit is given in the body of the text for material drawn from this bibliography.

Because of the uncertainty as to the author's authority for many statements, one would hesitate to recommend for general reading a book which discusses material concerning which, in many instances, statements are made that would indicate a final conclusion had been reached relative to problems which are still matters of controversy.

*Ten Years in the Congo* By W E Davis. 8°, cloth, 301 pp New York Reynal & Hitchcock, 1940 \$2.50

This is an interesting story of a missionary doctor, who spent ten years in the Belgian Congo. He came from the State of Washington, and entered the U S Army in 1917. After the war, he traveled extensively, and finally spent five years in Northwestern University Medical School. After an internship in Chicago, he went to the Congo. He was not, therefore, a trained missionary physician brought up under strict religious doctrines. He was apparently very successful in treatment of the natives, and the book gives an excellent account of his ten years' experience. He was an acute observer, and is a thoughtful narrator. The book should be widely read, for it makes an ideal volume for relaxation and broadens one's knowledge of medicine and of doctors in general.

Although hardly "a modern Dr Livingstone in the heart of Africa," as Dr Davis is referred to in the dust wrapper, there is no doubt that he thoroughly enjoyed his work and made a distinct contribution to the care of the sick and injured. At least from the point of view of those who stay at home, he can be congratulated on a fine narrative. This is one of the best books of its type that has come to the reviewer's attention within recent years.

# The New England Journal of Medicine

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VOLUME 223

AUGUST 22, 1940

NUMBER 8

## IS THIAMIN THE ANTINEURITIC VITAMIN?\*

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BOSTON

*But here the paralysis is to be referred to some affection of the muscles and not to the nerves — James Jackson. On a peculiar disease resulting from the use of Ardent Spirits. New Eng J Med and Surg 9:351-353 1822.*

A SURVEY of the recent literature would seem to indicate that most authorities on nutrition and also some neurologists have now accepted the truth of the theory that the polyneuritis of beriberi, alcoholism and other nutritional disorders is caused by deficiency of thiamin. The following quotations from recent reviews serve to illustrate the general acceptance of this theory.

The most constant and striking symptoms of a vitamin B<sub>1</sub> deficiency arise from degeneration in the nervous system. — Williams and Spies.<sup>1</sup>

Beriberi involves a peripheral nerve atrophy (the so-called "polyneuritis"). It can be cured or prevented by vitamin B<sub>1</sub>. — Harris.<sup>2</sup>

We now feel that the vitamin B<sub>1</sub> deficiency theory of the genesis of so-called "alcoholic" polyneuritis is proved. — Jolliffe.<sup>3</sup>

It is generally agreed that the peripheral neuritis of beriberi is caused by deficiency of this vitamin [B<sub>1</sub>]. — Wilbur.<sup>4</sup>

Clinicians have shown conclusively that peripheral neuritis may result from vitamin B<sub>1</sub> deficiency — Worts.<sup>5</sup>

If these statements are true, then polyneuritis of nutritional origin unassociated with evidence of other deficiencies requires no other treatment than the administration of pure synthetic thiamin. From the practical standpoint, this implication is obviously so important that it would seem worth while to reconsider carefully the evidence for the theory that thiamin deficiency is the cause of nutritional polyneuritis, before it passes on to be

included among the accepted doctrines of medical science.

In this article an attempt is made to re-evaluate the evidence from the previous literature, and to offer some new interpretations which may serve to show that the present theory of the causation of nutritional polyneuritis rests on a far less secure foundation than currently expressed opinions would suggest.

### EVIDENCE FROM LABORATORY INVESTIGATIONS

Ever since the earliest studies of the effects of vitamin B<sub>1</sub> deficiency in animals, the syndrome so produced has been considered as essentially similar to the human disease beriberi, just as black tongue in dogs is considered the animal counterpart of human pellagra. Eijkman<sup>6</sup> was the first to show that a disease characterized by disorder of the nervous system could be produced in fowls by feeding them a diet of polished rice, which also constituted the staple food of Javanese prisoners suffering from beriberi. When some years later this work came to be repeated, it was clearly demonstrated notably by Vedder and Clark,<sup>7</sup> that by suitable dietary means it was possible to produce in birds the anatomic changes of a true peripheral neuritis. These experiments were carried out before the differentiation of the vitamin B complex into more than one factor, and it is now certain in the light of present-day knowledge that the diets used were deficient not only in thiamin but also in the other components of the vitamin B complex. This peripheral neuritis, produced by a multiple deficiency, was rightly referred to as "polyneuritis gallinarum." Birds which developed this polyneuritis often showed evidence of marked disorder in the nervous system characterized by the signs of inco-ordination and opisthotonos. For this reason the development of these signs came to be regarded as sufficient evidence for the presence of the anatomic lesions of polyneuritis. When therefore, following the differentiation of vitamin

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B<sub>1</sub> from the remainder of the complex, it was subsequently shown that these signs also develop in animals deficient only in vitamin B<sub>1</sub>, the condition produced by vitamin B<sub>1</sub> deficiency was referred to as polyneuritis, notwithstanding the fact that the presence of peripheral nerve changes was never clearly demonstrated in pure vitamin B<sub>1</sub> deficiency.

Today it is quite evident that the inco-ordination and opisthotonos which develop in animals suffering from thiamin deficiency are not the result of anatomic changes in peripheral nerves. In the first place, these signs have an acute onset, which is so rapid that they could hardly be due to the development of structural changes in the nervous system. Secondly, it is now known that the signs disappear within a few hours on the injection of thiamin, indicating that they are due to a disturbance of function rather than of structure. Furthermore, it has been shown that animals which develop these signs may show no anatomic changes in the peripheral nerves,<sup>8-10</sup> and that when such changes occur (perhaps as the result of some other associated deficiency), they are apparently not influenced by thiamin therapy.<sup>9, 10</sup> The work of Peters<sup>11</sup> and his school has clearly demonstrated that the nervous signs of thiamin deficiency in pigeons<sup>12</sup> and rats<sup>13</sup> are the result of a metabolic disorder (or "biochemical lesion") of the nervous tissue involving a defect in the process by which pyruvic acid is normally removed. Similar signs may be produced in pigeons by other factors disturbing normal metabolism such as chloroform or insulin<sup>14</sup> and here there can be no question of any anatomic changes in the peripheral nerves.

It must be concluded that the signs by which thiamin deficiency in animals is ordinarily recognized are not the result of anatomic changes in the peripheral nerves, and that the fact that thiamin will cure these signs cannot be said to prove that thiamin is capable of curing polyneuritis in animals.

The foregoing argument must not be construed as implying that nutritional polyneuritis in animals is never the result of thiamin deficiency. Such a deduction would obviously be erroneous. Moreover, there is at least some theoretical evidence for thinking that thiamin deficiency might sometimes result in damage to peripheral nerves. It has been shown that thiamin is essential for the normal metabolism of nervous tissue, and although in acute deficiency few structural changes in the nerves are demonstrable, it is reasonable to suppose that the changes observed by Vedder and Clark,<sup>15</sup> and later by McCarrison<sup>16</sup> and by Kon and Drummond,<sup>17</sup> might result from prolonged

though partial deficiency of thiamin. This, however, is difficult to prove experimentally, since thiamin deficiency results in anorexia and probably other disturbances of the gastrointestinal tract which admit the possibility that defective assimilation and absorption of other factors contribute to the production of changes in the peripheral nerves.\* That such other factors might well play a part is clearly indicated by the fact that anatomic changes in the peripheral nerves have been reported to occur in several other deficiency cases in which the diet contained adequate amounts of thiamin. Mellanby<sup>18</sup> and Zimmerman and Cowgill<sup>19</sup> report demyelination of peripheral nerves in animals fed on a diet deficient in vitamin B<sub>1</sub>. Zimmerman, Cowgill and Fox<sup>20</sup> also report peripheral neuritis in dogs fed on diets adequate in vitamin B<sub>1</sub> but lacking only the other factors in the vitamin B complex. Moreover, similar changes may occur in animals suffering from simple starvation.<sup>21</sup>

From the evidence accumulating from laboratory data the following conclusions may therefore be drawn:

Thiamin is capable of curing a specific metabolic disturbance of the nervous system in animals. This disturbance has been incorrectly referred to as "polyneuritis" by many authors including myself.<sup>21</sup>

It is possible that chronic though partial deficiency of thiamin may result in true polyneuritis, but this does not appear to have been adequately demonstrated as yet.

There is as yet no clear experimental evidence showing that true anatomic polyneuritis in animals is curable by thiamin.

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Thiamin deficiency in animals disturbs not only the normal metabolism of the nervous tissue, but also, and in a similar manner the metabolism of the kidney, heart<sup>22</sup> and probably other organs. It so happens that the metabolic disturbance of the nervous tissue manifests

\*Since this paper was submitted for publication, Somo (Smith & Niles) has shown that thiamin deficiency in rats (Smith & Niles, 1937) has caused some cerebral but not spinal changes in the nervous system in thiamin deficiency. He has shown that in acute thiamin deficiency with opisthotonos the rats may show few or no structural changes, but that in chronic thiamin deficiency with opisthotonos and sometimes evidence of opisthotonos, degenerative changes are present in both the peripheral nerves and the spinal cord. Furthermore, he has demonstrated that once developed changes may undergo repair following the administration of thiamin in most of his cases, normal mixed grain. However, a point upon which this evaluates a direct causal relation between deficiency of thiamin and nerve degeneration. Apparently all the birds suffered from opisthotonos which is evidence of impaired digestion, and introduced the possibility that they were absorbing insufficient quantities of other factors from their diet. The improvement in digestion following treatment with thiamin might have an important influence in improving the absorption of other anatomic factors, and this may well account for improvement in the histologic appearance of the nerves.

self externally in a dramatic manner, while a similar disorder proceeding in the kidneys and elsewhere produces no such obvious effects. This has given rise to the erroneous belief that thiamin has a specific effect on nervous tissue. It is probably safe to say that thiamin is necessary for the normal metabolism of almost all tissues. For this reason, and for the reasons summarized above, it would seem that so far as the evidence from laboratory experiments is concerned there is really no great justification for referring to thiamin as the "antineuritic vitamin."

#### APPLICATION OF LABORATORY KNOWLEDGE TO CLINICAL PROBLEMS

Since the earliest differentiation of the vitamin B complex into heat labile ( $B_1$ ) and heat stable ( $B_2$  or G) fractions, the former has been thought of as having two outstanding characteristics: first that its deficiency in animals results in the signs of opisthotonos and inco-ordination (erroneously supposed to be evidence of anatomic polyneuritis) and secondly, that its deficiency in man results in the neurologic and cardiovascular manifestations of beriberi. In a similar manner vitamin  $B_2$  was considered to be the heat stable factor deficiency of which resulted in loss of weight in rats and the development of pellagra in man. Subsequent laboratory work resulted in the chemical isolation of the heat-stable substance which prevents loss of weight in rats, namely, riboflavin. However, it was soon found that riboflavin was not effective in the cure of human pellagra. Likewise, the pure substance thiamin which cures the nervous signs in animals, has now been isolated but it does not necessarily follow that thiamin is capable of filling the role of the hypothetical "anti beriberi vitamin."

Following the successful synthesis of thiamin by Williams and Cline<sup>22</sup> in 1936, this substance for the first time became freely available for clinical trial. As a result, there is now evidence that the cardiovascular manifestations of beriberi may be cured by pure thiamin.<sup>23</sup> But evidence for the direct etiologic relation of thiamin deficiency to the neurologic manifestations of beriberi is less definite, and ought not to be accepted without critical consideration. Before proceeding to consider this evidence, mention should be made of some further relevant observations:

Student courses in elementary physiology have usually taught that beriberi is due to lack of antineuritic vitamin  $B_1$ , just as surely as scurvy is due to deficiency of vitamin C. Nevertheless, there is reason to believe that the clinical manifestations of beriberi may result from deficiency of

more than one dietary factor. In the first place, it is worth remembering that human diets deficient in thiamin are almost inevitably deficient also in other components of the vitamin B complex. A diet consisting mainly of milled rice, such as is necessary to produce endemic beriberi in the Orient, also contains only small amounts of any of the factors in the vitamin B complex. Moreover, the neurologic and cardiovascular manifestations of beriberi as they occur in the Orient and among alcoholic subjects in this country, are frequently associated with stomatitis,<sup>24</sup> dermatitis,<sup>25</sup> anemia<sup>26</sup> and spinal-cord changes<sup>27</sup> that are clearly not due to lack of thiamin. This is important in view of the evidence from animal experiments that nutritional polyneuritis may result from deficiency of dietary factors other than thiamin. On practical grounds, it would be rather surprising if it so easily transpired that the two major manifestations of beriberi were in fact both due to thiamin deficiency and that the associated deficiencies played only a minor part in the development of this syndrome. As stated by Wolbach<sup>10</sup>: "In all probability some of the features of this disease, as commonly seen, are due to other deficiencies."

Following the chemical identification of thiamin in 1936, the term vitamin  $B_1$  has been generally regarded as synonymous with thiamin. Before that date, however, it was generally used by clinicians to mean no more than the hypothetical anti beriberi vitamin. For this reason any writings prior to 1936 in which specific claims were made for the etiologic relation of vitamin  $B_1$  deficiency to nutritional polyneuritis cannot with justification be quoted as expressions of the opinion that thiamin as now known was the factor concerned. Failure to appreciate this fact has led to several misinterpretations in recent literature.

#### CLINICAL EVIDENCE

##### *The Etiologic Identity of Alcoholic and Other Nutritional Neuritides with the Polyneuritis of Beriberi*

Evidence has accumulated during the last ten years to show that in several conditions other than beriberi a nutritional polyneuritis may occur having essentially the same etiology as in the disease originally attributed to vitamin  $B_1$  deficiency. The belief that lack of the anti beriberi vitamin may be the cause of polyneuritis occurring in a variety of diseases, including alcoholism was first expressed by Shattuck<sup>28</sup> in 1928. Minot, Strauss and Cobb<sup>29</sup> were the first to study in detail a large group of cases of so-called "alcoholic" polyneuritis. They concluded that dietary deficiency played an important etiologic role in this

condition, and "probably especially lack of [anti-beriberi] vitamin B<sub>1</sub>." Although pure thiamin was unavailable to these authors at the time, they are now quoted<sup>30</sup> as having shown that alcoholic polyneuritis is caused by lack of vitamin B<sub>1</sub> in the modern sense of the term, that is, of thiamin. Their observations and conclusions were supported by those of Meyer<sup>31</sup> and Wechsler<sup>32</sup>. Further evidence that alcoholic polyneuritis is primarily a nutritional deficiency was advanced by Strauss,<sup>33</sup> who showed that despite continued consumption of alcohol, patients with this disease showed clinical improvement when they received a nutritious diet together with various crude sources of the vitamin B complex. This was soon confirmed by the observations of Blankenhorn and Spies<sup>34</sup>. The opinions of all these authors are summed up in the statement by Strauss,<sup>33</sup> "Alcoholic polyneuritis may be regarded as similar to the polyneuritis of beriberi and treated accordingly," that is, by a high-vitamin, high-calorie diet, supplemented with yeast and liver extract to ensure a liberal supply of the hypothetical antineuritic factor. The efficacy of this treatment has lately been confirmed by Romano.<sup>35</sup>

In 1933, Strauss and McDonald<sup>36</sup> pointed out that polyneuritis of pregnancy responded well to similar treatment, and emphasized that this condition was essentially nutritional in origin and not due to toxins, as was then widely believed. They concluded "Polyneuritis of pregnancy is probably a dietary deficiency disorder similar to beriberi. Rational therapy should aim to supply the deficiency, which may be especially some portion of the vitamin B complex." The same conclusion was reached by Fouts and his collaborators,<sup>37</sup> who emphasized the importance of the vitamin B complex in curing this condition. Nevertheless, recent authors<sup>2, 5</sup> have cited these two groups of workers as having successfully treated the polyneuritis of pregnancy with vitamin B<sub>1</sub> (thiamin).

In a later review, Strauss<sup>38</sup> pointed out that disorders of the gastrointestinal tract are liable to give rise to "conditioned" deficiency disease, including the peripheral neuritis characteristic of beriberi. This review has been cited<sup>39</sup> incorrectly as showing that the neuritis in these deficiencies has been relieved by thiamin.

Thus far, then, the work of the pre-thiamin era was concerned with establishing the clinical and etiologic identity of nutritional neuritis occurring in beriberi, alcoholism, pregnancy and gastrointestinal disturbances. The emphasis throughout was to the effect that adequate treatment of these conditions consisted in the administration of foods rich in the vitamin B complex. When in some

cases a specific etiologic relation to vitamin B<sub>1</sub> deficiency was suggested, this implied no more than that these conditions were caused by deficiency of the hypothetical antineuritic vitamin, and it should not now be construed to mean that the authors believed nutritional polyneuritis to be due to deficiency of the pure chemical substance thiamin—a therapeutic agent entirely unavailable to them at the time.

### *The Relation Between Thiamin Deficiency and the Development of Polyneuritis*

In 1935, Jolliffe and his collaborators<sup>40</sup> advanced evidence in favor of a close relation between nutritional polyneuritis and deficiency of vitamin B<sub>1</sub>, in the sense of this term as then used by laboratory workers, that is, of thiamin. They accomplished the difficult task of obtaining from alcoholic addicts a sufficiently accurate dietary history to assess their consumption of thiamin and total caloric intake prior to admission. They used the formula,

$$\frac{\text{vitamin B}_1 \text{ (mg equiv)}}{\text{calories}} = 0.0000284 \times \text{body weight (gm.)}$$

which had been proposed by Cowgill on the basis of animal experiments in order to relate the thiamin requirements to caloric consumption and body weight. From this they concluded that polyneuritis occurred only in those subjects whose diet contained less thiamin than the amount called for by the estimated minimum requirement. However, this conclusion does not necessarily establish a causal relation between thiamin deficiency and polyneuritis. It should be remembered that diets deficient in one member of the vitamin B complex are almost certainly deficient in others. This is borne out by the observations of Elsom.<sup>41</sup> She also made use of Cowgill's formula in an experimental study on pregnant women in which the diets were carefully controlled, and showed that when the diet fell short of the estimated thiamin requirements macrocytic anemia developed, which indicated that the diet was then deficient in at least one other factor besides thiamin.

### *The Therapeutic Use of Thiamin in the Treatment of Polyneuritis*

Sufficient time has elapsed since synthetic thiamin first became available for clinical use to give opportunity for an adequate clinical trial. A critical appraisal of the results so far reported therefore seems justified. The task of reviewing all the literature on the use of thiamin in the treatment of nervous disorders could not be accomplished in the space of a single article. No attempt will therefore be made to assess the value

THAMMATH

[illegible]

+ reported improvement; 0 = reported decrease or improvement blank space = no report. Veget is an extract of yeast, and a potent source of the enzyme Vitamin B complex.

of thiamin therapy in the treatment of the neuritides of diabetes, leprosy, metallic and other toxic poisonings, postdiphtheritic paralysis, combined system disease, disseminated sclerosis, tabes dorsalis, herpes zoster, trigeminal neuralgia, chorea and poliomyelitis. Reference to the use of thiamin in these conditions will be found elsewhere.<sup>5-39</sup> This review will be limited to a discussion of the literature recently cited<sup>1-3, 39</sup> as demonstrating the beneficial effect of thiamin in the treatment of polyneuritis of definite nutritional origin,\* together with a few other references which are outstanding in their claim of the value of thiamin in the treatment of nonspecific neuritides, and therefore warrant careful analysis.

As Table 1 shows, the evidence for the cure of nutritional neuritis by thiamin therapy depends chiefly on the relief of symptoms. With the exception of the report of 3 cases by Jolliffe and Colbert,<sup>45</sup> there is only one attempt, that of Goodhart and Jolliffe,<sup>53</sup> to carry out a full analysis of the effect of this therapy in bringing about an alteration in the objective signs, both sensory and motor, of nutritional polyneuritis. These authors studied 17 patients with alcoholic polyneuritis whom they fed on a vitamin-rich diet supplemented by a potent source of the entire vitamin B complex (Vegex, an extract of yeast), in sufficient amounts to raise the estimated thiamin intake to four times the normal requirement. Eight of these subjects were given in addition 10 mg of thiamin intravenously daily. After ten days of treatment the improvement in these patients was compared with that in the remaining 9, who received diet and Vegex only. Of those who received only diet and Vegex, 2 improved in motor signs and 4 showed sensory improvement, whereas of those who received additional thiamin, 5 showed motor and 8 sensory improvement. (It is noteworthy that from the protocols given by these authors it would appear that after another six days 1 more of the first group showed motor improvement, and 3 more sensory improvement.) There are certain difficulties in accepting these results as definite evidence that thiamin is capable of relieving nutritional neuritis. In the first place, a study of this kind, which compares the rate of improvement in two groups of cases in both of which recovery is taking place, is liable to error unless a large number of cases are studied. Secondly, the additional thiamin might have had some influence in improving digestive function and facilitating the absorption of other antineuritic

factors present in the Vegex. Finally, the changes in physical signs observed must have been due to improvement in the function rather than in the structure of the nerves, since they took place in the short space of ten days, which would hardly be long enough to allow of much regeneration of degenerated nerve fibers.

Analysis of the remainder of the literature shows that in the majority of the other studies reported no mention has been made of the diet received by the patients. The possibility of other dietary factors contributing to the observed response can not therefore be excluded. Furthermore, in several cases the doses of thiamin given were so small as to raise doubts whether its administration had any significant influence on the clinical course.

The evidence throughout rests mainly on the relief by thiamin of the symptoms of pain, weakness and inability to walk. Unpublished observations by myself, based on a study of 2 alcoholic patients with polyneuritis who were fed a vitamin B-free diet and received intramuscular thiamin without other medication, confirm the impression that thiamin may have a marked effect in the relief of muscle pain and tender calves in nutritional polyneuritis. But in these cases there was no associated improvement in the objective neurologic signs, and the relief of the pain cannot be taken as evidence of improvement in the neuritis. There seems to be good evidence for the belief that this pain has in fact little to do with the associated anatomic changes in the peripheral nerves. The character of this type of pain and its related symptoms have been described by Strauss<sup>46</sup> as follows:

Heaviness of the legs and tenderness of the calf muscles when they are squeezed are usually the earliest manifestations. Walking short distances is unimpaired, but when longer walks are attempted weakness may become apparent. Frequently patients will note that they will commence walking with no disability whatever but that after having traversed a variable distance their legs will suddenly collapse under them. At first a distance of a mile or more may be required to bring out this weakness. Later a hundred feet may be sufficient. After some minutes of rest, walking can be resumed.

A similar description of this pain as it occurs in endemic Oriental beriberi has been given by Platt and Gin.<sup>56</sup> "Patients complain of severe aching pain in the legs after walking, the ease with which the pain is induced being some index of the severity of the disease. Moreover, the degree of recovery from beriberi can be estimated roughly in those cases without marked muscular atrophy by the distance they can walk before pain develops." These authors then add the following significant statement, "Our clinical observations taken

\*One paper<sup>42</sup> which has been quoted<sup>1, 3</sup> in illustration of the value of thiamin in the treatment of polyneuritis of pregnancy will not be reviewed here since in the 2 cases described therein the patients apparently suffered from pain due to obstetric trauma rather than to polyneuritis.

together with the views expressed on the metabolic basis of the disease suggest that the mechanism of pain production is similar to that following ischemia described by Lewis and his collaborators.<sup>10</sup> It is important to point out that thiamin is known to be concerned with the normal metabolism of carbohydrate, and that deficiency of this vitamin results in a disturbance in the normal path by which carbohydrate is broken down, and consequent accumulation of lactic and pyruvic acids in the tissues.<sup>11</sup> Since carbohydrate metabolism plays a very important part in providing the energy necessary for muscular work, deficiency of thiamin is probably as effective as partial anoxia in arresting the normal metabolism of muscle. I agree with Platt and Gin that the pain associated with true thiamin deficiency is primarily due to the same mechanism as that which produces ischemic pain, namely, the arrest of normal metabolic processes in the tissues. Thiamin by restoring these processes may relieve the pain but this is no evidence that it relieves the anatomic changes in the peripheral nerves which may also be present. Neuritis may be a factor in the production of this pain only in so far as the threshold for pain is probably lowered in demyelinated nerves, and hence the disturbed metabolism of the tissues induces an abnormally intense response of pain receptors.\*

It is noteworthy that Naide<sup>12</sup> has recently shown that the parenteral administration of large doses of thiamin sometimes relieves rest pain of ischemic origin. This observation may perhaps be explained on the ground that defective circulation hinders the normal supply of thiamin to the tissues, and that in this way their metabolism, which is already impaired by partial anoxia, becomes sufficiently disturbed to evoke pain. It is interesting to speculate whether impaired carbohydrate metabolism in diabetes mellitus may sometimes cause pain of an essentially similar nature, and whether such pain may contribute to the symptoms of diabetic neuritis. If this should prove to be the case, it is nevertheless unlikely that the administration of thiamin would relieve this pain, since the "biochemical lesion" in diabetes occurs at a

stage of carbohydrate metabolism remote from the point at which thiamin is known to act. In conformity with this theory, it may be mentioned that in spite of some reports in the literature of the beneficial effects of thiamin in the relief of diabetic neuritis, apparently no leading authority on diabetes has yet expressed agreement with these reports.

In view of the foregoing considerations and from the analysis of the literature given in Table 1 the following statements from recent articles appear to be scarcely justified at the present time

The clinician was thus provided with a method of approximating the vitamin B<sub>1</sub> requirement of man a knowledge of many factors modifying this requirement, and a therapeutic agent that could be administered *per os* or parenterally in pure form without incidentally furnishing other factors. With the use of these advances the clinician has been able in a period of three years to complete the evidence necessary to prove that many of the varieties of polyneuritis are caused by vitamin B<sub>1</sub> deficiency—Jolliffe.<sup>3</sup>

The treatment of polyneuritis of beriberi has become highly successful since the introduction of concentrated and crystalline forms of the vitamin.—Wilbur.<sup>4</sup>

Vitamin B<sub>1</sub> will usually relieve the manifestations of the polyneuritis of beriberi.—Spies et al.<sup>13</sup>

The feeding of thiamin is followed by re-myelinization and a return to normal in the microscopic appearance of the nerve trunks.—Vorhaus.<sup>14</sup>

Certain proof that thiamin will cure polyneuritis can only be achieved by a carefully controlled study in which all other factors of the vitamin B complex are excluded from the diet and thiamin alone is administered. If one is to judge by what is known of the rate of regeneration of degenerated nerve fibers,—traditionally stated to be 1 mm. a day—this experiment would have to be extended over a long period, and for this reason may never be undertaken.

It is perhaps unfortunate that physicians do not often report their negative results. If this custom were commoner present beliefs in the efficacy of thiamin in the treatment of nutritional neuritis might be less prevalent. However some disappointing results have been recorded (Ungley<sup>15</sup>). It is significant that apparently no optimistic reports have yet appeared on the use of thiamin in the treatment of the neuritis of endemic beriberi. A recent review from the Orient states, "Most workers seem agreed that the results of treatment of peripheral neuritis are much inferior to the treatment of acute cardiac beriberi" (Pallister<sup>16</sup>).

It is concluded that there is at present no proof that thiamin has any influence in effecting repair of nerve fibers which have suffered from degener-

In discussing the action of thiamin in the rapid relief of anemic symptoms, Spies and his collaborators<sup>13</sup> have recently stated "It is our thought that the initial prompt improvement with thiamin in cases of nutritional deficiency is hormonal in nature. This impression is furthered by the work of Minz who has been able to show that vitamin B<sub>1</sub> enhanced the effect of acetylcholine in the transmission of the nervous impulse. I assume that vitamin B<sub>1</sub> inhibits cholinesterase in the same manner as does physostigmine. In one case I in which this test was performed (I vitro) the serum cholinesterase was inhibited by the demethylation of thiamin."

It is noteworthy that Minz<sup>17</sup> specifically states that this alleged action of vitamin B<sub>1</sub> is not explicable by an inhibition of enzyme, but is due to a demethylation of the effect of acetylcholine on the cell. Apparently Spies and his collaborators have evidence to the contrary and for this reason the publication of their experimental data will be waited with interest. Yet it is difficult to see how excessive acetylcholine destruction can have much to do with the production of pain.

ation as a result of nutritional deficiency. However, there is evidence that thiamin relieves a certain type of pain and disability which, though frequently associated with peripheral neuritis, is primarily due to a different cause. This pain is usually most severe in the muscles of the legs, particularly after exercise, and is quite distinct from the symptoms which are primarily due to neuritis. The cause of the pain is a disturbance of function rather than of structure, it is brought about by a disordered or pathologic metabolism.

### COMMENT

Present beliefs concerning the relation of thiamin deficiency to the causation of nutritional polyneuritis are based on a misunderstanding between clinicians and laboratory workers. By longstanding tradition, laboratory workers have referred to the condition produced in animals by thiamin deficiency as polyneuritis. But they now know that there is no true peripheral neuritis in these animals, the physical signs being due to a disturbance of metabolism in the central nervous system. This disturbance is also present in other organs of the body, but it so happens that there it gives rise to no obvious external manifestations. The dramatic nature of the nervous signs and their spectacular relief by the administration of thiamin have given rise to the erroneous belief that thiamin plays a peculiar and specific role in the nutrition of the nervous system. And so it has come about that the vitamin has usurped the title of "antineuritic vitamin," which it in no way deserves. There is no definite proof at present that thiamin deficiency produces in animals the anatomic changes of a true peripheral neuritis, and certainly no evidence that thiamin will cure the peripheral neuritis produced in animals by other deficiencies.

In view of this misunderstanding, — the responsibility for which is shared by myself, — it is not surprising that when synthetic thiamin became available, clinicians were misled into thinking that this was the antineuritic vitamin which would cure nutritional neuritis in animals and presumably also in man. Perhaps this error might have been pointed out by the laboratory workers had it not been for the fact that very optimistic reports of the clinical value of thiamin in human nutritional neuritis soon began to appear. The laboratory workers, accepting the judgment of clinicians in clinical matters, were gratified to learn that thiamin relieved polyneuritis in man, although they had no evidence that it did so in animals.

Meanwhile the reports of clinicians were being

founded on the fact that thiamin appeared to relieve the pain and weakness associated with nutritional polyneuritis. However, there is reason to think that these symptoms are not primarily due to the neuritis, but to the same fundamental cause that gives rise to the nervous signs in animals, namely, a disorder of carbohydrate metabolism. As a result, both laboratory workers and clinicians have concluded from a similar misinterpretation of different evidence that thiamin will cure the anatomic lesions of polyneuritis.

When the literature of the last ten years is considered in perspective, the conclusion is inescapable that thiamin has never deserved the title of "antineuritic vitamin," and has not yet shown it self capable of filling completely the role that was formerly assigned to the hypothetical antiberiberi vitamin.

The exact deficiency responsible for nutritional neuritis remains obscure. Quite probably it is usually a multiple deficiency involving several dietary factors, of which thiamin may be one. But there is still a possibility that the true antineuritic vitamin has yet to be discovered.

### CONCLUSION

The polyneuritis associated with alcoholism, pregnancy and gastrointestinal disturbances is unquestionably due to nutritional deficiency, and is in every way similar to the polyneuritis of Oriental beriberi. But, contrary to numerous statements in recent literature, it has not been demonstrated that this polyneuritis is due to deficiency of thiamin.

For this reason it is of paramount importance that the treatment of nutritional polyneuritis should include an ample and nutritious diet, together with the administration of such preparations as yeast and crude liver extract to ensure an adequate supply of the entire vitamin B complex. The efficacy of this treatment has been established by sound clinical experience. Sometimes additional thiamin is beneficial, particularly in the cure of the cardiovascular disturbances of beriberi, and in the relief of the muscular pain and weakness which frequently accompany nutritional polyneuritis.

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OBSERVATIONS ON PRURITUS ANI\*

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**P**RURITUS ani is one of the most distressing conditions involving the anal region, and the least amenable to treatment. This paper offers no new remedy, but describes the various treatments tried in 175 cases seen during the last four years at the Rectal Clinic of the Massachusetts General Hospital.

ETIOLOGY

The exact etiology of pruritus ani is not definitely established. There are many theories, but not one of them explains all the facts. Local pathologic conditions such as fissure, fistula, hemorrhoids and cryptitis, allergic manifestations, reflex phenomena from a distant irritative focus, products of decomposition such as indole and skatole, fungous or local bacterial infection and dietary intolerance—each of them, singly or in combination with others, has been considered the true etiologic factor. In most cases there probably are several factors. The anatomic distribution of the lesions of pruritus ani suggests that the offending agent comes out of the anus in the form of a liquid or gas, and probably comprises one or more of the by-products of normal or defective digestion. In support of this theory is the presence of redness and burning of the perianal skin after several loose bowel movements, this undoubtedly results from the action of strong digestive juices from the upper intestinal tract that have reached the anus before their chemical nature has been altered. The acute skin irritation observed around most ileostomy and some colostomy openings is due to the same factor. Acute perianal dermatitis with itching occurring after anorectal operation is another example, the offending agent in this type of case is an irritating discharge from the infected wound. It is possible that the sensitivity of the skin varies in different patients and that only those with pronounced sensitivity develop pruritus. Many patients at the Rectal Clinic stated that itching started with the passage of feces or even flatus. A woman patient discovered that, although she had no visible discharge from the anus, if she kept her menstruation pad fastened tightly against the anal orifice she remained free from pruritus, whereas if she did not do so itching invariably occurred. In this case it seems

probable that the absorbent material of the pad took up the offending agent and prevented it from remaining in contact with the skin. In well established cases, the leathery redundant skin fold at the anal margin prevent efficient closure of the orifice and undoubtedly allow constant seepage. Mechanical irritation due to scratching and subsequent infection aggravate the condition. Local pathologic conditions such as fissures, cryptitis and hemorrhoids were present in 40 per cent of our cases. In numerous cases, however, the co-existing disease was corrected without relieving the pruritus or improving it permanently.

SYMPTOMS

Symptoms vary from the burning of an acute dermatitis, associated with erythema of the perianal skin, to a constant itching, in chronic, intractable cases. Erythema, vesiculation and excoriation are often seen superimposed on a thick leathery skin. Remissions of itching are common. For no apparent reason, several months or years may pass without any itching, and skin change may disappear only to return again at some future date.

STATISTICAL REVIEW

The age of the patients in this series varied from eighteen to eighty. There was only 1 below twenty while the third, fourth, fifth and sixth decade were about equally represented. Table 1 shows:

TABLE 1 Age Incidence (155 Cases)

Age	No. of Cases
yr	
Below 20	1
20 to 30	30
30 to 40	38
40 to 50	35
50 to 60	34
60 to 70	14
70 to 80	3
Total	155

the age incidence in 155 cases. The ratio of men to women was almost 2:1. The reason for this we consider to be the more scrupulous hygiene which women patients employ after defecation.

The duration of symptoms varied from one week to thirty years, as is shown in Table 2.

There was local disease in 40 per cent of the cases. This consisted chiefly of internal hemorrhoids.

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rhoids and external skin tags Table 3 shows the various accompanying conditions found in 140 cases. Itching of the skin in other parts of the body was present in 19 of the 175 patients

TABLE 2. *Duration of Symptoms (138 Cases)*

PERIOD	No. of CASES
Below 1 mo.	8
1 to 6 mo.	17
6 to 12 mo.	25
1 to 2 yr.	21
2 to 5 yr.	31
5 to 10 yr.	24
10 to 20 yr.	9
20 yr. and over	3
Total	138

The vulva and labia were involved in 11 cases, the pubes, thighs, groin or scrotum in 6. One patient had hay fever and 1 generalized dermatitis venenata.

### TREATMENT

There is no specific treatment for pruritus ani. Each case should be treated individually by one method or a combination of several. Scrupulous hygiene is of paramount importance. This includes

TABLE 3. *Concomitant Disease (140 Cases)*

CONCOMITANT DISEASE	No. of CASES
Internal hemorrhoids	31
External tags	10
Fissure	5
Anal aphthae	2
Fissure and hemorrhoids	1
Fistula and tags	1
Fistula and hemorrhoids	2
Infected crypts	1
Melanosis coli	1
Diverticulosis and hemorrhoids	1
None	84
Total	140

washing with soap and warm water after every bowel movement, and thorough drying without excessive rubbing.

### Local Applications

For topical applications the following medications have been tried

Calamine lotion  
Hamamelis water (witch-hazel water)  
Boric acid ointment  
Salicylic acid and sulfur ointment (6 per cent each) 10 petrolatum  
Castor oil (12 per cent), zinc oxide (18 per cent) and phenol (1 per cent) 10 lanolin  
Nupercaine ointment, 1 per cent  
Obtundia cream  
Scott's solution  
Tincture of Metaphen  
Tincture of benzoin

Silver nitrate, 10 per cent

Resorcinol (2 per cent), benzoic acid (2 per cent) and thymol (1 per cent) in alcohol (95 per cent)

These various medicaments are either soothing, astringent, antiseptic, keratolytic or anti-pruritic. Most cases respond to one or another.

Many simple early cases can be cured with nothing more than careful hygiene. Acute stages of erythema, excoriation and vesication without chronic skin changes can be made to disappear in one or two weeks by the application of Scott's solution or Tincture of Metaphen daily. Even cases that present signs of an acute dermatitis superimposed on chronic skin changes should be so treated. In the chronic cases showing thickening and discoloration of the skin without superimposed acute irritation, keratolytic and antipruritic ointments should be used. The application of salicylic acid and sulfur ointment is effective. With good hygiene, and by continued use of this or a similar ointment improvement may be rendered permanent.

### Injection Treatment

When all simple treatments fail, that is, hygienic astringent and antiseptic lotions and keratolytic and antipruritic ointments, we resort to some form of subcutaneous injection in order to interrupt the afferent sensory pathways. It was necessary to use injection treatment in 48 cases. Eighteen cases were injected with a solution containing quinine and urea hydrochloride and novocain. Sixteen were injected with an oil soluble anesthetic, and 14 with alcohol. No injection treatment should be carried out in cases with acute exacerbations.

*Quinine and urea hydrochloride* Eighteen cases were injected with a solution containing quinine and urea hydrochloride, 0.75 per cent, and novocain, 0.175 per cent.<sup>1</sup> The entire perianal area was treated at one sitting. The solution was injected subcutaneously through two punctures, one on each side 4 cm. from the anal margin, 10 to 15 cc. of the solution being used for each side. Only partial relief was obtained, but even this result was quite satisfactory to the patient. Anesthesia usually lasted for three or four weeks, while 3 patients experienced partial relief for as long as six months. In 2 cases with acute exacerbations no relief was obtained. Injection was repeated in a few cases, but after the third or fourth injection there was so much fibrosis beneath the skin that further injections were almost impossible. There was no sloughing in any of the cases and there were no painful reactions.

This type of treatment did not seem to be very effective

**Oil-soluble anesthetic** Sixteen cases were treated by injection of an oil-soluble anesthetic. The solution used was that recommended by Gabriel,<sup>2</sup> consisting of 0.5 per cent Nupercaine, 10 per cent benzyl alcohol and 1 per cent phenol in oil of sweet almonds. Under aseptic precautions, the oil was injected subcutaneously by means of a 10-cc Luer-Lok syringe and a 22-gauge needle, 1½ inches long. Either one or two quadrants were injected at weekly intervals, using about 5 cc of oil for each quadrant. One slough took four weeks to heal. The immediate results were very satisfactory on account of the almost complete anesthesia obtained. On the average, relief was complete for three weeks and partial for two or three weeks longer, after which recurrence invariably took place. Marked subcutaneous fibrosis occurred after three or four weeks, making a second attempt to inject oil almost impossible. This gradually disappeared after three or four months.

**Alcohol** Fourteen cases were injected with 70 per cent alcohol as described by Haskell and Smith.<sup>3</sup> One quadrant was treated at a time at weekly intervals. All the patients were ambulatory. The perianal area was washed with soap, dried and painted with Scott's solution or Tincture of Metaphen. The quadrant to be treated was infiltrated subcutaneously with 2 per cent novocain through a 26-gauge needle puncture 4 cm from the anal margin. Five cubic centimeters of novocain was used and massaged thoroughly to diffuse the solution in order not to dilute the alcohol. The novocain must be injected well beyond the limits of the proposed alcohol injection in order to ensure complete anesthesia. Through the same needle puncture 3 to 5 cc of alcohol was injected, taking good care to distribute the solution evenly and thus to prevent pooling. The alcohol should be injected into the subcutaneous tissue. If at any point it is injected into the skin, necrosis is sure to occur. There is considerable burning, which may last several hours after the wearing off of the novocain anesthesia. This is relieved by hot packs. There is redness and induration for a few days. A slough is to be expected in one out of four injections, but it usually consists of nothing more than a small area of skin necrosis. This should be allowed to heal before further injection is attempted.

Our results were satisfactory in 7 out of 10 cases. In 4 cases only two quadrants were injected. Three of these patients did not return.

This may mean either that they had complete relief or that they had much pain and were afraid to return. The fourth patient appeared one year later with itching in the quadrants not previously injected. Of the 10 cases in which the injection of the perianal skin was complete, 5 followed for over a year showed satisfactory results. These patients had anesthesia for two or three months. All had occasional itching after three months, but it was very mild compared with what it had been before. All the patients stated that their itching was only 10 to 15 per cent of its previous intensity. One other patient was followed four months, and was well at the end of that time. Another was followed only two months and was symptom-free. One case recurred at the end of four months. Two cases were complete failures, one had previously been injected with alcohol, and the other with Gabriel's solution. The patients obtained relief for only a few weeks.

#### X-Ray Treatment

Of the 4 patients treated by x-ray, 1 obtained relief for seven weeks, 1 for three weeks, 1 had no relief and 1 had partial relief for a year.

#### CONCLUSIONS

Each case of pruritus ani should be treated as an individual problem. Most of the early cases do well with carefully regulated hygiene and soothing lotions. Chronic cases with acute exacerbations improve when painted with Tincture of Metaphen or Scott's solution. The acute dermatitis clears up in one or two weeks, and good hygiene prevents a recurrence in many cases. In chronic cases with skin thickening, keratolytic or antipruritic ointments are often sufficient. In about one fourth of our cases all simple treatment failed and some form of injection was necessary. Subcutaneous injection of 70 per cent alcohol gave the best results in this group.

#### SUMMARY

The etiology of pruritus ani is discussed. Statistics on 175 cases are given. The various forms of treatment are summarized. Results of the injection of quinine and urea hydrochloride and novocain, Gabriel's solution and 70 per cent alcohol are reported.

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## THE TREATMENT OF GONOCOCCAL INFECTION IN WOMEN\*

## A Comparison of the Results with and without Sulfanilamide Therapy

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CHICAGO

GONOCOCCAL infection in women is more widespread and a far more serious infection than it is in men. Its complications, sterility, obstinate infection and invalidism, are responsible for a major part of the work of the gynecologist. Gonorrhea occupies a unique position among acute infectious diseases, not only in its clinical manifestations but in the fact that the organism, the gonococcus, has certain special inherent characteristics that differentiate it very conspicuously from other pathogenic bacteria. There exists no immunity to the gonococcus, either from previous infection or by individual resistance or racial qualities.

The gonococcus has a selective action for certain mucous surfaces, and when deposited on these grows immediately and profusely in the same manner as do other bacteria on their favorite soil. No injury to the surface of the tissue is necessary for its growth and reproduction. The organism is exclusively a human parasite, and is with difficulty grown on species other than man. The gonococcus is sensitive to both heat and cold and is very fragile out of its normal or cultural environment. In the presence of other bacteria in a culture the diplococcus is readily crowded out. From a clinical standpoint one of the unusual peculiarities of a gonococcal infection is its power of latency. The organism can remain in the tissues for months in an apparently dormant state until stimulated into activity by some change in the circulation in the surrounding tissue. This renewed activity can be produced by local trauma, childbirth, menstruation, pelvic operation, excessive venery or systemically by some other infection or by alcohol. The exacerbation of a chronic infection may present all the symptoms of a fresh invasion. For the development of a gonococcal infection the tissue on which the organism is deposited must be of special epithelial structure, it must be moist and the blood supply abundant. The tissues most frequently invaded are those of the urethra, Skene's glands, cervix, Bartholin's

glands, fallopian tubes, peritoneum, rectal mucosa and the conjunctiva.

During the eight year period 1930-1937 we used in the treatment of gonococcal urethritis and cervicitis local instillations of 1 per cent silver proteinate in a 4 per cent gelatin mixture. This was given each day for two or three weeks. We are of the opinion that by the addition of gelatin to the medicament the drug is held in closer contact with the tissue—a surface tension phenomenon. The gelatin seems to possess the power to take up the toxic products,—exotoxins and endotoxins,—and in this manner to diminish the irritating quality of the discharge and at the same time presumably increase the beneficial action of the drug. Oral medication consisted of the ingestion of 10 minims of sandalwood oil three times a day after meals. Patients with a concomitant rectal infection were given suppositories containing 1 per cent silver proteinate in oil of theobroma. These were inserted following each bowel movement. In patients who had suffered a pelvic extension, rest in bed, application of heat to the lower abdomen and intramuscular injections of a foreign protein were productive of good results. At the first sign of pelvic involvement which usually occurs at about the time of the menstrual period, all local treatment was discontinued and vaginal examinations were omitted. Douches were not prescribed at any stage of the infection, as they do little good at any time and may be distinctly harmful.

We have reviewed 241 case records of patients treated by this method. In this series 230 patients were Whites and 8 were Negroes. One hundred and one were married, 32 divorced, 21 separated, 8 widows and 79 single. The youngest patient was sixteen years of age, and the oldest fifty-two. The average age was twenty-eight. Forty-six patients gave a history of a previous gonococcal infection.

The tissues found to be infected are shown in Table 1. The infection if primary in the urethra was rarely limited to this site, and the reverse was true of cervical involvement. In many cases more than one area was involved at the time of admission.

\*From the Women's Division of the Public Health Institute, Chicago, Ill.

†Director, Urological Division, Public Health Institute.  
‡Staff member, Gynecological Department, Public Health Institute.

One of the most distressing complications of gonorrhea in women is extension to the fallopian tubes. Despite any and all forms of treatment, the number of women suffering from this invasion is large. There were 92 patients, or 40 per cent, in this group who had a salpingitis, in 10 of whom it was present on admission. There were 15 patients who developed an infection of Bartholin's gland. None of these infections were bilateral. Only 2 patients had an arthritis, and in

TABLE 1 Infected Tissues in 241 Cases Treated without Specific Chemotherapy

INFECTED TISSUE	No. OF CASES
Urethra	173
Cervix	193
Rectum	96
Bartholin's gland	15
Tubes	92
Joints	2

both cases the sexual partner suffered the same complication. In this connection, having observed a number of similar cases we have concluded that the condition may be due to a special strain of the gonococcus which has a selective affinity for the articular surfaces of the joints. We never apply a splint or cast in these cases, and in only 1 case has there been any loss of joint function, due in this case to lack of co-operation by the patient.

The uncomplicated cases were under treatment or observation for an average of one hundred and one days, with an average of thirty-five visits for treatment and observation. The average length of time before the vaginal smears became negative and remained so was ninety-seven days. Seven weekly smears were examined before the patients were dismissed.

In the group of patients who had a pelvic infection the average period of treatment was one hundred and thirty days, and an average of ninety-seven days elapsed before a negative smear was obtained. While the average number of weekly observation smears taken in the cases without complications was six, the number in the cases of salpingitis was nine.

In taking smears as criteria of cure we secure at least two before and at the completion of a menstrual period. All treatment procedures are omitted when these tests are being made. After a patient is dismissed from treatment we urge her to refrain from sexual intercourse for at least three months, but direct that should she expose herself all possible precautions are to be taken before and after the act. All patients are advised to return in three months for a re-examination. Ninety-six

patients (40 per cent) did so, and all were found to be free of gonorrhea.

In a group of 241 cases in which the patients received the same local therapy but were given sulfanilamide orally, there were 230 Whites and 11 Negroes. Seventy-eight were married, 32 divorced, 32 separated, 17 widows and 82 single. The youngest was seventeen and the oldest fifty-one. The average age was twenty-seven. There were 25 patients who admitted a previous gonococcal infection.

The tissues found to be infected are shown in Table 2. A large number of patients had the in

TABLE 2 Infected Tissues in 241 Cases Treated with Specific Chemotherapy

INFECTED TISSUE	No. OF CASES
Urethra	156
Cervix	152
Rectum	97
Bartholin's gland	22
Tubes	36
Joints	1

fection in the urethra and cervix at the time of admission. Gonococci were found in the rectal smears in 97 cases. Gonococci were only rarely isolated from the rectum without organisms' being found in the urethra or cervix or both. There were only 32 patients (13 per cent) with a salpingitis, an incidence which is nearly three times less than that in the group treated by the older method. The infections of Bartholin's gland in this group were double the number found in the previous series, however, we cannot explain this finding.

The uncomplicated cases were under treatment and observation for an average of sixty-five days. This represents an improvement of about 35 per cent when sulfanilamide is administered. The average length of treatment and observation for the complicated cases was seventy days, an improvement of almost 50 per cent in comparison with the first classification (Table 3). One of the

TABLE 3 Comparison of Results with and without Sulfanilamide Therapy

DATA	METHOD OF TREATMENT	
	WITHOUT SULFANILAMIDE	WITH SULFANILAMIDE
Average number of days under treatment and observation		
Uncomplicated cases	101	65
Complicated cases	130	70
Average number of treatments before smears remained negative	28	17

surprising phenomena noted was that the patients who were able to take only 20 gr of sulfanilamide daily made almost parallel progress with those

taking larger doses. We have no satisfactory explanation for this observation, unless it be that the concentration of the drug in the blood has not the significance previously attributed to it in relation to the control and cure of gonorrhea. Forty two patients (17 per cent) were unable to take sulfanilamide in doses of any size. In 29 of these cases the medicament was omitted from the treatment plan, as the reactions were of sufficient severity to interfere with the occupation of the patient. In 5 cases the drug caused a dermatitis which was not dangerous but was very disturbing to the patients. In an additional 45 cases the dosage was reduced from 40 to 20 gr daily without the elimination of annoying reactions.

#### SUMMARY AND CONCLUSIONS

This study purports to show that the modern management of gonococcal infection in women with sulfanilamide and topical applications halves the distressing pelvic complications and reduces the length of time of treatment by a third. We observed an increase in the number of abscesses of Bartholin's gland but can give no satisfactory explanation for this finding. However, the complication is of minor importance in so serious an infection. The reactions to sulfanilamide are numerous but usually of a minor nature. Seventeen per cent of the patients were unable to take 40 gr of the drug without disturbing reactions.

159 N Dearborn Street

## NEW HAMPSHIRE MEDICAL SOCIETY

### PROCEEDINGS OF THE

### ONE HUNDRED AND FORTY NINTH ANNIVERSARY

House of Delegates, May 13, 14 and 15, 1940

(Continued from the issue of July 25)

#### *Report of the Committee on Medical Economics*

The Committee on Medical Economics has given its consideration to three problems during the year.

**Farm Security Administration Insurance Program.** In pursuance of the instructions given it by the House of Delegates at its annual meeting your committee studied the proposals of the Farm Security Administration relative to health insurance for its clients, and made recommendations for the guidance of any county societies contemplating the plan. These recommendations were transmitted to the several county secretaries.

The program for general practitioner care is now in operation in Grafton and Cheshire counties, having gone into effect January 1, 1940. The Sullivan County Society at first approved the proposals, but later rescinded its action and withdrew from the plan. Obviously the length of time that the plan has been in effect is too short to justify any conclusions regarding it.

**Sickness Insurance.** Because of the widespread interest among lay governmental and medical circles in the problem of the distribution of medical care, and because of the particular emphasis among members and groups of the profession in some form of insurance as an answer to the problem, your committee has begun a study of this question.

The intricacies and complexities of the problem are manifold, as attested by the large number of differing plans which are now in operation under the supervision of state and county medical societies, and by the long and expensive investigations conducted by several state societies before any satisfactory conclusions could be reached.

Your committee is not prepared to make any recommendations regarding sickness insurance in New Hampshire. It does recommend that the study be continued with a view to observing the operation of the various plans

now in effect and for the purpose of drawing up a plan which would be applicable in New Hampshire if the need should arise.

**National Physicians Committee for the Extension of Medical Service.** Your committee believes that the solving of the problem of the adequate distribution of medical care is of urgent and vital importance. It further believes that the National Physicians Committee for the Extension of Medical Service is composed of able and upright leaders of the profession who are making a vigorous attack on this problem.

Your committee, therefore, recommends that the House of Delegates approve the activities of the National Physicians Committee for the Extension of Medical Service and urge its members to accord this committee their active moral and financial support.

LESLIE K. STAMORE,  
RICHARD W. ROBINSON  
CLARENCE E. DUNBAR.

**DR. ROBERTSON.** The Committee on Officers Reports recommends that this committee's recommendation, with respect to the continuation of the study of sickness insurance, be adopted.

We further approve the recommendation relative to the National Physicians Committee for the Extension of Medical Service, and recommend that this action be reported to that committee and to the members of the Society urging their active, moral and financial support.

I move the adoption of this portion of our report.

This motion was seconded and was carried.

### *Report of the Committee on Tuberculosis*

The program for the control of tuberculosis has progressed to the point where our goal at this time is to conquer the disease so completely that it will be eradicated from the human family. Eradication is not now a hoped for possibility but an actuality which can be won, in the considered judgment of leaders in preventive medicine throughout the nation. Sound basis for this conclusion is the tremendous progress already gained in the control of the disease, the increasing effectiveness of treatment, and the definite resources available for early discovery of cases.

Our greatest difficulty today, as in the past, is to find the people who have tuberculosis. Eighty per cent of the patients admitted to the New Hampshire State Sanatorium during the past year were moderately advanced or late cases.

This vital phase of the campaign against the disease—the finding of the people who have tuberculosis—has grown in the past twenty years. Two important developments give additional encouragement to physicians, public health workers and others engaged in the task. The first—the tuberculin test—tells us whether or not a person is infected with tubercle bacilli. The second—x-ray study of the chest—demonstrates early pulmonary lesions. We urge that the tuberculin test and x-ray study of positive reactors be accepted and carried out as a routine procedure in hospitals and in general practice.

Your committee again reminds you of its willingness to be of service in the matter of interpretation of chest x-ray films sent in for readings.

The Vollmer patch tuberculin test is now being used in the tuberculosis clinics as a routine procedure. The comparative studies made so far as to the relative reliability of the patch test and the standard intradermal protein purified-derivative (PPD) test indicate that the former is equal to the latter in its effectiveness as a diagnostic index of the presence or absence of tuberculous infection. Of 6000 comparative testings reported in the studies throughout the country, New Hampshire reported 1455. The intradermal test is still being used in the tuberculin test and chest x-ray demonstrations conducted by the New Hampshire Tuberculosis Association among the high school groups. However, in the regular diagnostic clinics the patch test is used.

We realize that the cost of treatment of tuberculous patients has increased because of the increase in the use of surgery in treatment, and that the cost of the discovery and prevention of tuberculosis has increased because of the necessary employment of tuberculin tests and chest x-rays. We emphasize here, however, as no doubt we have in previous reports, that an adequate investment now to speed up and hasten the control of tuberculosis will be self liquidating and final.

ROBERT B KERR,  
ROBERT M DEMING,  
JOHN D SPRING

DR. ROBERTSON. The Committee on Officers' Reports urges the physicians of New Hampshire to use the tuberculin test more freely.

I move the adoption of that portion of our report.

This motion was seconded and was carried.

### *Report of the Committee on Child Health*

Your committee held scheduled meetings on September 1 and November 10, 1939, and March 16 and May 3, 1940.

Last year we stated that the *Report of the Committee on Immunization and Therapeutic Procedures for Acute Infectious Diseases* of the American Academy of Pediatrics, for which we had received an appropriation of \$50, was out of print. This year a revised, larger report was printed, and this was sent to each member of the Society. Your committee endorses wholeheartedly the recommendations of the committee of the American Academy of Pediatrics.

Subsequent experience is bearing out the value of tetanus toxoid, particularly for people who are allergic and therefore not good subjects for horse serum. We believe that this should be used more widely, either plain or mixed with diphtheria toxoid.

We previously reported an interest in the health standards of summer camps. We note with approval that the Department of Health has ruled that only pasteurized milk may be used in these camps.

Your committee has continued to work in close cooperation with the Division of Maternal and Child Health and the State Board of Health. The following activities were carried out by the Division of Maternal and Child Health and the Division of Crippled Children at the suggestion and with the help of your committee:

1. A consultation service utilizing two pediatricians appointed by the State Board of Health was instituted during the fiscal year. The duties of these consultants are as follows: to serve local physicians by acting as consultants on pediatric problems, to evaluate the conduct at existing child health conferences and to aid in the setting up of conferences, to advise in the selection of literature on subjects of child health for free distribution to the public, to aid in the teaching program to lay and professional groups concerning matters of value in problems of child health and pediatrics, to conduct teaching child health conferences, to evaluate and aid in the working out of conference forms, such as records, at child-health conferences, and to carry out such other advisory services in the field of child health as may be presented.

2. The library of educational films dealing chiefly with subjects of child health and child behavior has been enlarged. The recent purchase of the film "Life Begins" had the endorsement of the committee.

3. Increased activities were carried out in the educational program by extension to lay groups of talks concerning the value of breast feeding, nutrition of the child and helpful points concerned with infant feeding.

4. Efforts to use the two-dose toxoid in the immunization against diphtheria in preference to the one-dose alum precipitate and the discontinuation of performing Schick tests, except in certain special cases, were adopted as a policy.

5. Wider free distribution of silver nitrate to local physicians and to hospitals for use in the eyes of the newborn was recommended.

6. The utilization of pediatricians at crippled-children's clinics, to ensure better care of the child and a general health appraisal, was advised.

7. Wider free distribution of vaccines, especially smallpox vaccine, to physicians requesting them was recommended. This is in line with our previous rec-

commendation in attempting to facilitate the practice of preventive medicine in the office of the doctor instead of having all people in the low income group of necessity availing themselves of free clinics.

The advice of your committee was helpful in the preparation by the Department of Health of the pamphlet on summer camps. We were able to bring to the attention of the department the work of some of the members of the Academy of Pediatrics along this same line.

Your committee has again endeavored to keep in the closest possible touch with progress in pediatrics by attendance of individual members at regional and national meetings of the American Academy of Pediatrics through representation on the council of the New England Pediatric Society and by attendance at meetings of the national public-health organizations.

COLIN C. STEWART  
TRAVIS P. BURROUGHS,  
FRANKLIN N. ROGERS.

DR. ROBERTSON The Committee on Officers Reports moves the adoption of this report.

This motion was seconded and was carried

### Report of Necrologist

The following deaths have occurred during the past year

1939		
NAME	PLACE OF DEATH	DATE
Walter A. Allen	Haverhill Massachusetts	August 23
Lloyd H. Cogswell	Warner	November 25
Charles F. Flanders	St. Petersburg Florida	November 12
Bert D. George	Rochester	May 21
Alpha H. Harriman	Laconia	May 30
Elmer E. Lake	Hampstead	December 6
Alfred A. Macleavy	Manchester	June 1
John J. Mulvanity	Boston, Massachusetts	August 13
H. Scott Pattee	Manchester	August 26
Guy D. Tibbets	Antrim	June 2

1940  
Alfred Bielschowsky Brooklyn New York January 5  
HENRY H. ARSDEN

DR. ROBERTSON I move the acceptance of this report of the necrologist

This motion was seconded and was carried

DR. CHESTER L. SMART We have received a communication from the Joint Committee on Professional Relations, which includes the Medical Society of New Jersey and the New Jersey Pharmaceutical Association. This letter was with reference to a resolution which was sent to us last year but which was not acted on. The resolution is as follows:

RESOLVED That the Joint Committee on Professional Relations request the Medical Society of New Jersey and the New Jersey Pharmaceutical Association to enter a formal protest against the prescribing of medicines and the giving of medical advice on the radio, with the exception of such broadcasts on health matters

as are given under the auspices of recognized associations of licensed physicians or federal, state and local health departments and be it further

RESOLVED That such protest be sent to the broadcasting companies and the Federal Communications Commission.

DR. ROBERTSON Your committee recommends the adoption of this resolution

This motion was seconded and was carried

DR. DUBE I have a communication from the Works Progress Administration, and the following recommendations are made

1 That the Society approve the paragraph relative to injury cases requiring medical treatment. (Injury cases requiring medical treatment shall be distributed among qualified physicians in as equitable a manner as possible. Injured employees may indicate their personal preference as to physicians and such preferences may be honored where the physician is qualified and the selection will not materially disturb the equitable distribution of cases among available physicians.)

2 That we believe these cases are equitably divided now

3 That it is inadvisable and financially impracticable at this time for the New Hampshire Medical Society to have a committee or individual make monthly surveys and reports to the Works Progress Administration at Washington D. C.

I move the adoption of these resolutions.

This motion was seconded and was carried

DR. SMART The University of New Hampshire is having its seventy-fifth anniversary next year

DR. BLOOD I move that the Society accept the invitation to co-operate, and that a committee of three, one of whom shall be the president, be appointed to confer with the University

The motion was seconded and was carried

DR. SMART I move that Dr. Blood, Dr. Wilkins and the incoming president be the ones to confer with the University of New Hampshire

The motion was seconded and was carried

DR. SMART We have a final communication here on the medical emigrés

I move that the President the Secretary and the three other members of the Public Relations Committee consider and be given power to act on this communication

This motion was seconded

DR. DEERING G. SMITH You say "power to act", does it mean that these men can recommend or not recommend? I think it would be much safer to table the whole thing. The present state law takes care of new applicants.



The motion before the House was withdrawn

DR SMART I move that the matter of medical emigrés be tabled

This motion was seconded and was carried

DR HENRY O SMITH The Trustees of the New Hampshire Medical Society present a recommendation for action by the House of Delegates That recommendation is made by unanimous vote

The Board of Trustees of the New Hampshire Medical Society recommends to the House of Delegates that the sum of \$2000 be given to the trustees of Dartmouth College, to be used in helping defray the costs of sorely needed equipment for the medical school, this amount to be taken from the accumulated income of the Bartlett Fund, which can be used only "for the benefit of medical science."

DR FREDERIC P LORD I second that motion

DR SMITH For the information of any of the members of the House of Delegates who may not be familiar with the facts, let me make a brief statement

The will of Dr Josiah Bartlett, Jr, probated one hundred and two years ago this month, gave to the New Hampshire Medical Society the sum of \$200, to be placed at interest for ten years, and "the product of which, with the original sum, to be a permanent fund, the annual income to be expended for the benefit of medical science as may be directed by a vote or votes of said society"

But one gift has been made from the income of this fund, now amounting to over \$6000—a grant of \$1000 made thirty-six years ago to aid in the construction of a new building for the Dartmouth Medical School This school now urgently needs additional facilities for the departments of physiology and pathology, and it seems to me very fitting for this society to take the initiative in meeting this need

Drs Josiah Bartlett, Sr, Josiah, Jr and Josiah 3rd, all served as presidents of this society, Josiah, Jr., the donor of this fund, for seven consecutive years Their connection with the Dartmouth Medical School is evidenced by the fact that to each one Dartmouth College granted the degree of M.D

I believe that in no way can we more fittingly honor the memory of Dr Josiah Bartlett, Jr., than by the grant of this sum from the income of the fund left to us by him

The motion was carried

DR DEERING G SMITH I have a resolution in the matter of the increasing activities of state laboratories

WHEREAS, The continued growth and development of that special branch of medicine known as clinical pathology is necessary for the proper diagnosis and treatment of the sick and is essential to the science and practice of medicine, and

WHEREAS, The growth of laboratories of state boards of health has been abnormally augmented by grants-in-aid from the Federal Government, and

WHEREAS, The effect of these grants-in-aid is to extend these services to all citizens without regard to their ability to pay, and

WHEREAS, The excessive development of laboratory medicine by state boards of health serves as an entering wedge for state-medicine practice, which apparently will include all medical specialties, and

WHEREAS, These practices will inevitably result in the curtailment of the practice of clinical pathology, which is essential for the continued growth and development of clinical pathology, and tend to discourage young, well-trained physicians from entering this essential field, be it therefore

RESOLVED, That the House of Delegates recommends to all state medical societies that they hold conferences with the authorities of the state boards of health with the view of limiting the services offered by the laboratories of these organizations (in general, laboratory services by the state board-of-health laboratories should be confined to requests made by health officers or others in authority representing municipal, township, county and state public health and welfare organizations, and to requests made by physicians whose patients find it difficult or impossible to pay for the cost of laboratory services of this kind in the customary manner, in general, laboratories of the state boards of health should not provide services at taxpayers' expense to persons who are able to provide for themselves), and be it further

RESOLVED, That the House of Delegates of the American Medical Association, through the Council on Medical Education and Hospitals and the Section on Pathology and Physiology, undertake an educational campaign to set forth these problems to the medical profession

I suggest that this be referred to the Committee on Memorials and Communications

SPEAKER FERNALD I appoint the following for the Committee on Nominations Deering G Smith (chairman), Henry C Sanders, Jr., Charles H Parsons, Francis J C Dube, Earl J Gage

If there is no further business to come before the meeting, a motion is in order to adjourn

DR DYE I move that we adjourn

This motion was seconded and was carried

Whereupon, the first meeting of the House of Delegates was adjourned at 10 45 p m

\* \* \*

The House of Delegates convened at the Hotel Carpenter, Manchester, on Tuesday morning, May 14, at 8 30 with Speaker Fred Fernald, of Nottingham, presiding

The following members answered the roll call

The President, ex-officio  
 The Vice President, ex-officio  
 The Secretary-Treasurer, ex-officio  
 Chester L. Smart, Laconia  
 Earl J. Gage, Laconia  
 Francis J. C. Dube, Center Ossipee  
 W. J. Paul Dye, Wolfeboro  
 Norris H. Robertson, Keene  
 Leander P. Beaudoin, Berlin  
 Lewis C. Aldrich, Jefferson  
 Leslie K. Sycamore, Hanover  
 John C. Eckels, Lisbon  
 Frederic P. Lord, Hanover  
 Deering G. Smith, Nashua  
 Henry O. Smith, Hudson  
 Clarence E. Dunbar, Manchester  
 George V. Fiske, Manchester  
 Clarence E. Butterfield, Concord  
 Warren H. Butterfield, Concord  
 Fred Fernald, Nottingham  
 Frederick S. Gray, Portsmouth  
 James Sanders, Rye  
 Edna Walch, Dover  
 Henry C. Sanders, Jr., Claremont

**SPEAKER FERNALD** Has Dr. Smart a report to make?

**DR. SMART** I have a report on the resolution that was read last night. There is a perfectly good reason why the pathologists should want such a resolution. One can understand that it is only fair, in many ways, that they should have it. But, some of the men, even last night, said that they were having a great many Wassermann tests done, for instance, which certainly would not be done if their patients had to pay for them. After all, that is a rather important thing and if passing a resolution like this is going to cut down that type of diagnostic medicine, I think we should give it careful consideration before we recommend it.

**DR. DUBE** Might I ask Dr. Burroughs to tell us what examinations are made in this State?

**DR. TRAVIS P. BURROUGHS**, Concord We have three laboratory units of the State Board of Health: one is a chemistry unit at the State House, another is a bacteriology and serology unit at the State House, and the third is a bacteriology unit at Hanover.

We are not doing any tissue pathology. As I understand it, the laboratories of the Dartmouth Medical School have been doing tissue pathology for a number of years, but at least no tissue pathology is being done for or on behalf of the State Board of Health.

On the serological side, we are doing blood tests for syphilis, for undulant fever and for one or two other diseases, such as typhoid fever. On the bacteriological side, we are doing tests for com-

municable diseases. We are not doing any pregnancy tests.

One of the outstanding pieces of laboratory work that we have been doing in communicable diseases has been the typing of pneumococci. You will recall that two or three years ago, the House of Delegates called on the State Board of Health to start a pneumonia program, largely because of the reason that antipneumococcus serum was so costly that a great many people were not getting serum treatments, and because those who could pay for it were rather inclined to put off treatment until such a time as it was not effective.

It is unfortunate that antipneumococcus serum is effective for only one or two out of thirty-two possible types, and it is also unfortunate, in spite of what the detail men of the supply houses tell us, that it is a very difficult thing to type pneumococci accurately.

On account of the experiences they have had in Massachusetts and other places where pneumonia programs have been in progress quite a while, it was essential that the State should do the laboratory work on the basis of which it issued its serum or else it should make a check against laboratory work which was reported to it, in connection with a request for specific serum. That is one of the points where the work of the laboratory has increased markedly.

The other thing that has increased under federal grants-in-aid has been the matter of the blood testing for syphilis. Blood testing is absolutely a part of the program for the detection of cases of syphilis, and, as you know, the detection of cases of syphilis and getting them under treatment are the only ways we have of cutting down the incidence and prevalence.

Another thing in connection with the blood testing for syphilis is that all the tests are difficult so much so that the people who have been evaluating the efficiency of laboratories doing such tests have come to the conclusion that no laboratory should attempt to do them unless it is doing at least fifty specimens a week. I do not believe there are many laboratories in New Hampshire that have an opportunity to do fifty specimens a week. Hence, unless there is going to be a series of private laboratories established specifically for the purpose of testing syphilis, the State Laboratory is probably the most convenient place to send specimens.

Another part of the syphilis blood-testing program which has expanded tremendously, has been in connection with the various things the State has required. As you know, the Legislature has required that every applicant for marriage

license shall have a Wassermann, Kahn, or some similar standard laboratory test for syphilis. It is specifically set forth in the law that that shall be done, without charge, by the State Board of Health. That was one of the reasons that the law was passed. I am quite sure if it had not been stated to the Legislature that those examinations would be made without charge to the applicant, there would have been enough votes to have prevented the law from passing.

We also have the matter of the annual blood testing of hairdressers, and the annual blood testing of barbers. Those are not matters of law, but of regulation.

I should like to bring up one other point here, because it has been a matter of discussion for a number of years. I refer to the distinction between the practice of medicine and the practice of laboratory technology. It is our intention, in the State Laboratory of Hygiene, not to practice medicine, and the laboratory people have specific instructions that they are not to make diagnoses.

You will recall that when the premarital blood-test law was put through, it was specifically stated that marriage should not depend on whether the Wassermann was reported positive or negative by the laboratory, but should depend on whether the physician, certifying as to the applicant, said that the applicant should or should not be permitted to marry.

I feel that the answer is this. The laboratory should stick to laboratory work, and leave the diagnosis and treatment to the physician. I do not believe that, under those circumstances, it is necessary, from a technical point of view, to have the laboratory work done by a physician.

SECRETARY METCALF I move that this matter be laid on the table.

This motion was seconded and was carried.

DR SYCAMORE Every year, there comes before the House of Delegates a number of questions of policy which are quite important. Frequently, these questions have a lot of implications, the average delegate does not have a chance, in the time the questions are before the House, to consider the implications and to make any decision of his own.

I move that the chairman of the Committee on Officers' Reports and the chairman of the Committee on Memorials and Communications each be instructed to submit to the Secretary not later than two weeks before the annual meeting, a statement of any questions of policy which will be brought before the House of Delegates in the report of their committees, and I further move that

the Secretary be instructed to add to these lists a statement of any similar questions of which he has knowledge and transmit the complete list to each member of the House of Delegates in advance of the annual meeting.

The motion was seconded and was carried.

DR SANDERS I wish to bring up for reconsideration the motion that the round-table conferences be continued.

It has come to my knowledge that there are a number of members of the Society who do not especially like these round-table discussions, and they would have, preferably, the old type of meeting, with papers. I move the reconsideration of the vote taken last night.

This motion was seconded and was carried.

DR DYE Inasmuch as the motion to reconsider has been carried, I should like to make a motion that each member of the Society be polled, with a return postal card.

This motion was seconded and was carried.

SPEAKER FERNALD Is there any further business to come before this meeting?

If not, a motion is in order to adjourn.

DR DYE I move that we adjourn.

This motion was seconded and was carried.

Whereupon, the second meeting of the House of Delegates was adjourned at 9.30 a.m.

\* \* \*

The House of Delegates convened at the Hotel Carpenter, Manchester, on Wednesday morning, May 15, at 8.30, with Speaker Fred Fernald, of Nottingham, presiding.

The following members answered the roll call.

The President, ex-officio  
 The Secretary-Treasurer, ex-officio  
 Chester L. Smart, Laconia  
 Earl J. Gage, Laconia  
 Leander P. Beaudoin, Berlin  
 Lewis C. Aldrich, Jefferson  
 Leslie K. Sycamore, Hanover  
 John C. Eckels, Lisbon  
 Frederic P. Lord, Hanover  
 Deering G. Smith, Nashua  
 Henry O. Smith, Hudson  
 Clarence E. Dunbar, Manchester  
 George V. Fiske, Manchester  
 Clarence E. Butterfield, Concord  
 Warren H. Butterfield, Concord  
 Fred Fernald, Nottingham  
 Frederick S. Gray, Portsmouth  
 James Sanders, Rye  
 Edna Walch, Dover  
 Henry C. Sanders, Jr., Claremont

**SPEAKER FERNALD** Our first order of business this morning is the report of the Committee on nominations

### Report of the Committee on Nominations

#### MEMBERS

**President** Ezra A. Jones John Z. Shedd, Richard E. Wilder

**Vice-President** Charles H. Dolloff John A. Hunter Henry C. Sanders Jr.

**Councilor for Merrimack County** (five years) Henry H. Amsden.

**Councilor for Hillsborough County** (five years) Clarence O. Coburn.

**Trustee** (three years) Frederic P. Lord

**Speaker of the House of Delegates** Robert O. Blood.

**Vice-Speaker of the House of Delegates** Timothy F. Rock.

**Neurologist** Henry H. Amsden.

**Delegate** (American Medical Association 1941-42) Deering G. Smith.

**Alternate Delegate** (American Medical Association, 1941-42) Emery M. Fitch.

**Delegates** (New England state medical societies, 1940) as printed in program

#### PENDING COMMITTEES

**Amendments to Constitution and By-Laws** James B. Woodman Chester L. Smart, Frederick S. Gray

**Control of Cancer** George C. Wilkins, Howard N. Kingsford, George F. Dwnell

**Medical Economics** (three years) Leslie K. Syca more.

**Medical Education and Hospitals** (three years) John P. Bowler

**Mental and Social Hygiene** Charles H. Dolloff Benjamin W. Baker, John B. McKenna

**Publication** Carleton R. Metcalf Warren H. Butterfield, Ellsworth M. Tracy

**Public Relations** The President, the Vice President, the Secretary-Treasurer Robert J. Graves, Joseph N. Friberg

**Scientific Work** Carleton R. Metcalf Frederic P. Scribner Nathan T. Milliken.

**Tuberculosis** Robert B. Kerr Robert M. Deming M. Dawson Tyson.

#### SPECIAL COMMITTEES

**Child Health** Colin C. Stewart, Jr., Travis P. Burroughs, Franklin N. Rogers.

**Maternity and Infancy** Robert O. Blood, Benjamin P. Burpee, Marion Fairfield.

**Medical Relief** Robert J. Graves John P. Bowler Roland J. Joyce.

DEERING G. SMITH  
HENRY C. SANDERS JR.,  
CHARLES H. PARSONS,  
FRANCIS J. C. DUBE  
EARL J. GAGE.

**SPEAKER FERNALD** The next order of business is voting, by ballot, for president. I appoint the following as tellers to collect and count the votes Clarence E. Dunbar and Frederick S. Gray

The ballots were cast and counted

**DR. DUNBAR** Eighteen votes were cast for Ezra A. Jones

**SPEAKER FERNALD** Ezra A. Jones is elected president for next year

The next order of business is the election of the vice president by ballot.

The ballots were cast and counted

**DR. DUNBAR** There were eighteen votes cast, one for Dr. Hunter, five for Dr. Sanders and twelve for Dr. Dolloff

**SPEAKER FERNALD** Charles H. Dolloff is elected vice president for next year

**DR. LORD** I move that the Secretary cast one ballot for the rest of the nominations submitted by the Committee on Nominations

This motion was seconded and was carried

**SECRETARY METCALF** The Secretary has cast the ballot.

**SPEAKER FERNALD** I declare the rest of the slate, as submitted by the Committee on Nominations, duly elected

**DR. WILKINS** In 1932, when I was president of the Society, there was a change in the by-laws which created the Benevolence Fund. At that time, the original amendment provided for \$1 a year being taken from the dues of each member to be applied to the Fund. The amendment was changed by the House of Delegates to 50 cents. That means that during these years, there has been approximately \$250 paid in each year for this fund. Now at the end of eight years it has reached only the sum of \$2300.

It was too late yesterday to offer an amendment to increase the amount to \$1 to be added each year, but that will be brought in next year. Dr. H. O. Smith has suggested that it would be possible to take \$1000 from the General Fund, and transfer it, if the House of Delegates is willing.

My motion is that the Trustees be instructed to transfer at least \$1000 from the General Fund to the Benevolence Fund.

This motion was seconded and was carried

SECRETARY METCALF Gentlemen, I move that we express our gratitude to the Manchester group of doctors for the work they have done this year, and I suggest, if they are willing, that they take up the burden again for 1941

This motion was seconded and was carried

SECRETARY METCALF I move, also, that we express our thanks for the work that Dr Harris E Powers has done, and the large amount of

time that he has given to the Society for this meeting

This motion was seconded and was carried

SPEAKER FERNALD If there is no further business, a motion is in order to adjourn

DR COBURN I move that we adjourn

This motion was seconded and was carried

Whereupon, the 1940 meeting of the House of Delegates was adjourned at 9 20 a.m

## REPORT ON MEDICAL PROGRESS

### THE TREATMENT OF THE ARTHRITIDES OF KNOWN ORIGIN\*

WALTER BAUER, M.D.,† AND CHARLES L. SHORT, M.D.‡

BOSTON

LAST year's progress report<sup>1</sup> having been devoted to the classification and diagnosis of the various arthritides, it seems appropriate that the one for this year should deal with the treatment of joint diseases of known etiology. The management of articular disorders of unknown cause will be discussed in a subsequent report.

The physician must ever be aware that accurate diagnosis is a prerequisite for the successful treatment of articular diseases. His diagnostic skill is greatly enhanced if he follows a useful classification of articular diseases.

#### TRAUMATIC ARTHRITIS

Under traumatic arthritis is included strain, sprain, intra-articular derangements, traumatic synovitis and fracture into the joint. We must not forget that trauma may determine the localization of either specific infectious or rheumatoid arthritis, initiate an acute phase of degenerative joint disease or precipitate an acute attack of gouty arthritis.

The treatment of an acute traumatic arthritis depends on its location as well as on the type and severity of the injury sustained. Restoration of the anatomic relation of the articular and periarticular structures by conservative or operative treatment

is most important. Following this, immobilization and complete physiologic rest by means of adhesive strapping, splints, plaster casts or other suitable apparatus are indicated. The joint should be kept at complete rest until muscle spasm and effusion have disappeared. Normal joint motion and muscle strength are finally restored with the aid of carefully supervised physiotherapy.

The application of heat or cold may relieve discomfort. Painful effusions should be aspirated. In such cases examination of the synovial fluid is of diagnostic value. An acute traumatic effusion rarely contains more than 1000 leukocytes per cubic millimeter, with polymorphonuclears ranging from 0 to 20 per cent. Erythrocytes are frequently observed. In some cases frank intra-articular hemorrhage will be detected. Following aspiration, a compression bandage should be applied.

For more detailed instructions pertaining to the treatment of acute joint injuries, one should consult a surgical or orthopedic textbook. Failure to institute adequate therapy of the type outlined may result in chronic joint disability, characterized by pain, chronic effusion, loss of normal joint function, muscle atrophy and finally post-traumatic monoarticular degenerative joint disease.

#### SPECIFIC INFECTIOUS ARTHRITIDES

The advent of sulfanilamide has established beyond all doubt that effective chemotherapy against microbial disease is possible. The introduction of sulfanilamide and allied compounds in the treatment of many of the specific infectious arthritides

\*This is publication No. 49 of the Robert W. Lovett Memorial for the Study of Crippling Disease. Harvard Medical School.  
From the Medical Clinic, Massachusetts General Hospital, the Department of Medicine, Harvard Medical School, and the Massachusetts Department of Public Health.

The arthritic studies in this clinic are made possible in a large part by a grant from the Commonwealth Fund, New York City.

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‡Instructor in medicine, Harvard Medical School, assistant physician, Massachusetts General Hospital.

represents the greatest advance ever made in the treatment of joint disease. With specific therapy available for many of these arthritides, there should be less need for surgical drainage, better end results, fewer days of illness and less economic loss. Since orally administered, relatively inexpensive compounds have proved most effective in the treatment of the specific infectious arthritides, all physicians should be thoroughly acquainted with the practical aspects of their administration. Contraindication to their use, dosage, toxic reactions and the types of joint disease in which they are indicated will be taken up as the treatment of each form of specific infectious arthritis is discussed.

### *Tuberculous Arthritis*

There is no specific treatment for tuberculous arthritis. Because tuberculosis of the joints is only one manifestation of a tuberculous infection all authorities are agreed that rest for both the local lesion and the patient should be the keystone of all therapy. Good food, fresh air and hygienic surroundings are essential. Heliotherapy is a valuable adjunct in the treatment of tuberculous joints, but convincing proof is lacking that it alone is sufficient.

It has long been known that bony ankylosis results in the cure of a tuberculous joint, and this has been considered by many to be the most desirable end result. Unfortunately, it rarely occurs in the natural course of the disease. Surgical fusion of tuberculous joints with resulting bony ankylosis has gradually been accepted as the approved method of treatment, despite the fact that it met with widespread opposition at the time of its introduction. Some workers have contended that immobilization of an affected joint by means of a brace, plaster cast or other type of apparatus gives end results fully as good as those achieved through operative interference. The time required for cure by the latter method is longer and complete arrest of the disease process is less certain. The question of operative interference must always be decided on the merits of the individual case. In one case, arthrodesis might be beneficial, in another, the operation might be dangerous or useless. The reader who is interested in a more detailed discussion of the treatment of tuberculous arthritis should consult authoritative treatises.<sup>2-4</sup>

### *Gonococcal Arthritis*

The specific value of any therapeutic measure can be established only if one is able to demonstrate that the clinical course of the disease is strikingly altered by it in a large percentage of

cases. The results with sulfanilamide therapy indicate clearly that this drug is specific for gonorrhea and its complications. It has proved as efficacious as its much heralded predecessor, fever therapy. Its advantages over fever therapy are many.<sup>5,6</sup> Administration is much less complicated and does not require a special apparatus or a trained personnel. It is a less heroic and less dangerous form of therapy. The primary focus is more frequently cured with sulfanilamide therapy than it is with hyperpyrexia. Most important of all, it is relatively inexpensive and is therefore available for the treatment of all types of gonorrhea.

*General treatment.* A patient with gonococcal arthritis should be kept at rest in bed if a weight-bearing joint is involved, or if either fever or sulfanilamide therapy is administered. The diet is not important, it should be well balanced and suited to a patient with an infectious disease. The fluid intake is regulated in accord with the type of therapy employed, fluids are forced in the patient receiving no specific therapy or hyperpyrexia and are restricted when sulfanilamide is given. An acutely inflamed joint may require complete rest in a splint or cast. Pain due to marked intra-articular distention may be relieved by aspiration. Analgesics or opiates may be necessary until relief is obtained from specific therapy.

*Sulfanilamide and sulfapyridine therapy.* The only absolute contraindication to the administration of sulfanilamide is a known hypersensitivity to the drug,<sup>7</sup> but liver disease, blood dyscrasias and renal disease usually contraindicate its use.<sup>8</sup>

The dose of sulfanilamide administered and the regularity with which it is given are extremely important if one is to obtain the largest possible percentage of cures. Many of the reported failures have resulted from improperly administered or inadequate doses of the drug or from failure to keep the fluid intake constant. *In treating patients with sulfanilamide the desired blood level must be maintained. This can be achieved only by administration of the drug every four hours day and night and by maintenance of a constant fluid intake.* The observance of this simple rule is imperative because sulfanilamide is as readily excreted by the kidney as it is absorbed by the gastrointestinal tract.<sup>9,10</sup> A total twenty-four hour fluid intake of 1500 to 2000 cc. is adequate for most patients with gonococcal arthritis receiving sulfanilamide. Maintenance of a constant fluid intake, provided it is not excessive, is more important than the amount allowed for any twenty-four hour period. An excessive intake results in an increased urinary output, which in turn reduces the blood sulfanilamide to a lower level than that expected from the dose given. If an excessive

intake is allowed, a larger dose of the drug will be required to maintain the desired concentration of sulfanilamide in the blood

We advocate large doses of sulfanilamide in the treatment of gonococcal arthritis, believing that this mode of administration ensures the highest percentage of cures.<sup>5-10</sup> *The dose is calculated in the following manner 0.05 gm ( $\frac{3}{4}$  gr) per pound of body weight, provided the total dose does not exceed 8 gm.* The calculated dose represents the amount to be given each day following the initial twenty-four-hour amount

The dose having been calculated, the drug is administered orally in one of two ways. One half the calculated dose is given initially and again in four hours, then one sixth the calculated dose is administered every four hours, day and night, or one sixth the calculated dose is given initially and every four hours. When the drug is given according to the first schedule, a blood sulfanilamide level of from 10 to 15 mg per 100 cc or higher results, whereas the second schedule allows for the maintenance of a blood sulfanilamide level of between 5 and 10 mg per 100 cc

Although sulfanilamide cures are experienced when the blood sulfanilamide level remains as low as 3 to 5 mg per 100 cc throughout the period of therapy, it has been our experience that more cures are obtained when the level is maintained at 10 mg or higher. This is extremely important in such a serious gonococcal complication as arthritis, which may go on to joint destruction

The exact length of time the drug should be administered depends largely on the patient's response. In mild cases where the joint symptoms clear rapidly and gonococci can no longer be demonstrated by culture or smear in the genitourinary focus, the dosage may be reduced by one third or one half in the second week. In severe cases full dosage had better be continued for at least two weeks. In most cases of gonococcal arthritis, marked improvement is noted within forty-eight to seventy-two hours. If such improvement is not observed, the dose of the drug should be increased, if necessary until a blood sulfanilamide level of 20 mg per 100 cc has been obtained. If the arthritis shows no apparent response to sulfanilamide therapy once such blood levels have been obtained, the diagnosis should be carefully checked. There is always the possibility that such failures result from sulfanilamide-resistant gonococcal strains or failure of some inherent host factor to play its usual role. Those patients who fail to respond to large doses of sulfanilamide can subsequently be treated with sulfapyridine or fever therapy. Our present rule is to try sulfapyridine

Sulfapyridine should be administered as follows: 2 gm initially and in four hours, then 1 gm every four hours during the first twenty-four hours, then 1 gm every four or six hours, day and night. This dosage should be continued for at least one full week. If improvement results, the dose can be reduced by one third or one half during the second week. The clinical reports to date have not shown that sulfapyridine is superior to sulfanilamide in the treatment of gonococcal arthritis, provided the latter drug is given in adequate doses. Uleron (sulfanilyl dimethyl sulfanilamide) is not so effective and may produce peripheral neuritis.

Parenteral administration of sulfanilamide is very rarely indicated in acute gonococcal arthritis, except in the rare case complicated by pelvic peritonitis or meningitis, because the drug is usually well tolerated by mouth. This is most fortunate, because it is practically impossible to maintain a constant blood sulfanilamide level when the drug is administered parenterally.

Because of the regularly occurring acidosis encountered in sulfanilamide therapy, certain workers<sup>7-11</sup> have advocated the administration of regular doses of sodium bicarbonate in amounts up to 36 gm per day. The routine administration of sodium bicarbonate in the doses advocated would not begin to compensate for the alkali loss resulting from sulfanilamide therapy.<sup>12</sup> Its administration is optional and not imperative. In some cases it does seem to reduce somewhat the associated nausea and vomiting.

Sulfanilamide can be safely administered only if the patient is under careful clinical and laboratory observation. The red-blood-cell count and white-blood-cell count should be determined at least every three days. The patient should be carefully observed for the development of toxic symptoms, which have been very adequately described by various workers.<sup>7-13-14</sup>

The milder toxic symptoms do not indicate serious complications. Many of them represent the symptoms of acidosis. If the acidosis is marked, it can be relieved by large oral doses of sodium bicarbonate or racemic sodium lactate. When the acidosis requires parenteral therapy, a 1/6 M (molar) solution of racemic sodium lactate is the medication of choice. Varying grades of cyanosis are seen in all patients receiving large doses of sulfanilamide. It is not an alarming symptom and can usually be disregarded.

Fever develops in 10 to 15 per cent of patients.<sup>11</sup> It usually occurs during the first week of sulfanilamide administration. Omission of the drug results in its subsidence within thirty-six to forty-eight hours, thus proving that sulfanilamide and

not gonococcal arthritis or some other complication is responsible for the increased temperature. Since fever may be the first sign of severe hemolytic anemia, granulocytopenia, hepatitis or a skin eruption, it is obvious that fever constitutes the most important warning signal. In the absence of these complications, readministration of the drug may be tried in severe cases.

A severe hemolytic anemia may occur during the first week of treatment,<sup>13</sup> necessitating the immediate withdrawal of the drug and the use of transfusions. In many patients no alteration of the red-cell count is observed. Approximately one third of the patients develop a moderate anemia of a subclinical hemolytic nature,<sup>6</sup> accompanied by a reticulocytosis, and when the drug is discontinued a spontaneous gradual rise of the red cells and hemoglobin to the pre-treatment level occurs. Transfusions are rarely required and the drug need not be stopped unless the red-cell count falls below 3,000,000.<sup>6</sup> Provided the patient has been on a good diet, the use of liver or iron has not been shown to increase the speed of recovery. If the patient is already anemic before treatment is started, transfusions should be given before or with the administration of the drug.<sup>6</sup> In every case, the red-cell count should be done at three-day intervals during treatment.

Leukopenia and agranulocytosis may develop during sulfanilamide treatment,<sup>6, 14-17</sup> usually about the second week. If agranulocytosis develops the drug should be omitted and fluids forced, and transfusions may be necessary.

Skin rashes may result from administration of sulfanilamide and are associated with fever.<sup>7, 18</sup> Both usually disappear promptly on discontinuance of the drug. In certain cases erythema and edema may result from exposure to sunlight. For this reason patients receiving sulfanilamide should not be exposed to sunlight or ultraviolet radiation. Any skin complication is a contraindication to further sulfanilamide administration.

The occurrence of hepatitis as a toxic manifestation of sulfanilamide therapy has been reported,<sup>7</sup> and in some cases has terminated fatally. If this complication should arise, the drug should be discontinued, fluids forced and a high-carbohydrate intake prescribed.

The symptoms of sulfapyridine toxicity are the same as those of sulfanilamide, with the addition of the appearance of sulfapyridine crystals in the urine, hematuria, gross or microscopic, and anuria. The latter complications occur more frequently if the fluid intake is less than 2000 cc per day. Patients receiving sulfapyridine should have a urine examination every second day in addition to red-cell and white-cell counts.

*Fever therapy* Although the introduction of fever therapy marked a great advance in the treatment of gonococcal arthritis, it has fallen into disfavor because of the almost uniform response of such cases to sulfonamide compounds. Its use is still indicated in the occasional patient in whom the use of sulfanilamide and sulfapyridine is contraindicated or in whom sulfonamide compounds have failed. When employed it should be administered by a trained hospital personnel.<sup>19</sup> If this is impossible, artificial fever may be induced by typhoid vaccine intravenously.<sup>19</sup> In such cases the fever can usually be maintained by the use of hot water bottles and blankets.

Manipulative measures aimed at treating the primary focus during the acute phase should be omitted if possible in order to avoid a recurrent bacteremia and further extension of the arthritis although this danger is materially reduced if they are undertaken while sulfanilamide is being administered. There is no contraindication to combining the more simple procedures, such as irrigation and douches, with sulfanilamide therapy. That gonococcal vaccines and filtrates are efficacious in the treatment of gonococcal infections has never been proved. We do not employ them.

Once the joint has become painless and the inflammation has largely disappeared active motion is desirable in order to hasten the return of normal function. This can be accomplished by adequate physiotherapeutic measures and protection against unusual or faulty weight bearing. In patients in whom treatment was instituted too late to prevent permanent joint damage, more formidable orthopedic measures such as arthroplasty or arthrodesis may be necessary.

### *Septic Arthritis*

Although invasion of the articular cavity by any organism may result in a septic arthritis, staphylococci, hemolytic streptococci and colon bacilli are the commonest offenders. Such bacteria may reach the joint via the blood stream by direct extension from a neighboring focus or by way of a penetrating wound. The earlier the diagnosis is made, the better will be the therapeutic results. Early diagnosis must depend on aspiration and bacteriological examination of the fluid.

General treatment should be instituted early and should consist of immobilization of the joint repeated joint aspirations, analgesics or opiates if required, maintenance of a good dietary intake and a positive fluid balance, and transfusions if indicated. Once the bacteriological diagnosis has been established chemotherapy should be instituted. In the case of infection due to either the hemolytic streptococcus or the colon bacillus, sulfanilamide should



be used in the same dosage outlined under gonococcal arthritis. If improvement is not experienced within seventy-two hours, the dose should be increased, or sulfapyridine should be administered in full doses. The general condition of the patient, the appearance of the joint and the results of the analyses of the repeated synovial fluid aspirations will enable one to determine whether surgical drainage is required. The results to date indicate that there will be less need for surgical interference in the future than there has been in the past.

Sulfathiazole is probably the most effective chemotherapeutic agent at our disposal for the treatment of staphylococcal arthritis, although sulfapyridine has been reported to be effective in staphylococcal septicemia. Sulfathiazole should be administered in 1-gm doses every four hours, day and night. Once obvious improvement has been observed, the dose can be reduced to one half the amount. If the staphylococcal infection is not amenable to sulfathiazole therapy, free dependent drainage with the continuation of chemotherapy offers the best chance for a normal, movable joint.

Joint ankylosis due to septic arthritis may be treated by arthroplasty after it has been quiescent for several years.

#### *Pneumococcal Arthritis*

Pneumococcal arthritis is encountered as a complication of pneumococcus pneumonia in approximately 0.1 per cent of cases. The primary form is rare. Bacteriological examination of the aspirated synovial fluid is necessary for diagnosis. It should not be confused with the arthritis of serum sickness following the administration of antipneumococcus serum. In addition to good medical care, treatment consists of early immobilization, repeated aspirations and the administration of full doses of sulfapyridine. Chemotherapy will probably obviate surgical drainage, which was so often necessary in the past.

#### *Typhoidal Arthritis*

Typhoidal arthritis is a rare complication of typhoid fever. Suppuration and ankylosis of the involved joints rarely occur. The presence of typhoid fever, or a history of a recent typhoidal infection, with the recovery of organisms from the involved joints, establishes the diagnosis. This type of arthritis is seldom encountered because of the decreasing incidence of the disease. Fixation of the joint and repeated aspirations are probably the only forms of therapy indicated in most cases. The treatment of the spinal form of typhoidal arthritis consists in fixation of the spine with a plaster shell or brace until the process becomes

quiescent. Rarely is surgical interference necessary or indicated.

#### *Meningococcal Arthritis*

In severe meningococcal infections, usually accompanied by a hemorrhagic rash, multiple joints may become painful and tender, without associated marked swelling or effusion. Such joint symptoms are thought to be due to hemorrhages into the articular and periarticular tissues. They are transitory in nature, and their treatment is symptomatic.

The metastatic pyoarthrosis is a complication of meningococcal infection which usually appears at the end of the first week. It is usually monoarticular. Aspiration of the joint reveals the presence of meningococci in the synovial fluid. Treatment of this type of meningococcal arthritis consists of fixation, repeated aspirations and the use of sulfanilamide in adequate dosage. Rarely if ever is surgery indicated.

Chronic meningococcal septicemia often presents itself as a case of unexplained fever, with associated recurrent embolic rashes and intermittent migratory arthritis. Treatment should be directed toward the eradication of the systemic meningococcal infection, the joints being of secondary importance. Here again, sulfanilamide administration in adequate dosage is indicated.

#### *Syphilitic Arthritis*

The articular manifestations of congenital syphilis are known as Clutton's joints, or tenosynovitis syphilitica. The disease is self-limited and usually not influenced by treatment. Since the ultimate prognosis is good, whether treated or not, the importance of diagnosis lies first in the recognition of syphilis in the patient and his family, and secondly in distinguishing this form of joint disease from tuberculous or rheumatoid arthritis.

That an acute form of arthritis may be a manifestation of secondary syphilis has been proved by the demonstration of spirochetes in synovial fluid by rabbit inoculation. The diagnosis is rarely difficult. If rapid improvement does not ensue following the institution of antisyphilitic treatment, one should suspect that the patient is probably suffering coincidentally from some other form of arthritis.

Tertiary syphilis may involve any one of the joint structures. In rare cases biopsies may be necessary in order to distinguish tertiary syphilis from neoplastic disease of the bone. If the patient shows evidence of syphilis elsewhere or a positive Wassermann reaction, a trial of antisyphilitic therapy is indicated. If the existing lesion does not respond to such treatment, the diagnosis should be questioned.

Charcot joints secondary to *tabes dorsalis* will be covered in the section devoted to neuroarthropathies.

### *Arthritides Associated with Other Infectious Diseases*

Brucellosis may be accompanied by arthritis, the treatment of which should be aimed at the eradication of the systemic infection. Rarely, a suppurative arthritis secondary to an osteomyelitis is encountered. When present, it requires surgical drainage.

Arthritides associated with bacillary dysentery, Haverhill fever, Reiter's disease and the exanthemas, exclusive of scarlet fever, rarely if ever represent a serious complication. The treatment is symptomatic, consisting of analgesics, temporary fixation of the joint if necessary and aspiration for relief of pain due to articular distention.

The rare cases of arthritis in association with subacute bacterial endocarditis (*Streptococcus viridans*) are the results of septic emboli lodging in or around the joints. The inflammation usually disappears in a matter of days, suppuration does not take place, and specific measures are never necessary.

The joint manifestations of scarlet fever are of three distinct types. The acute type of polyarthritis represents the onset or reactivation of rheumatic fever. Its treatment is the same as that for rheumatic fever. The nonsuppurative type of arthritis, with sterile effusion, usually occurs during the first two weeks of the disease and is frequently migratory in character. It does not require specific therapy. The patient is made more comfortable by the judicious use of analgesics, heat and, occasionally, splinting. Septic arthritis due to the actual invasion of the articular structures by the hemolytic streptococcus sometimes occurs, usually in the second or third week of the disease. The treatment is the same as that outlined under septic arthritis.

Arthritis may be a manifestation of lymphogranuloma venereum. Because the arthritis is self-limited, evaluation of therapy is extremely difficult. Some success has apparently been obtained with sulfanilamide when administered in adequate dosage.<sup>20</sup>

### NEUROPATHIC ARTHRITIS (CHARCOT JOINTS)

Neuropathic joints are most commonly associated with *tabes dorsalis*, syringomyelia and leprosy, and rarely with injuries or with other diseases of the spinal cord and peripheral nerves. Whatever the origin, the management is the same. Anti-syphilitic medication is without effect in arresting the neuropathic arthritis associated with *tabes dor-*

salis. The treatment of the neuroarthropathies is for the most part an orthopedic problem, and includes the use of braces and other forms of apparatus. When weight-bearing or spinal joints are involved, early fusion is the method of choice and offers the best chance of arresting the disease process. In syphilitic neuroarthropathy antisyphilitic therapy should be administered before and after surgical interference. If any form of apparatus is used it should be well padded in order to prevent pressure sores.

### GOUTY ARTHRITIS

The history alone should suggest the correct diagnosis in the majority of patients suffering from gouty arthritis. It is generally agreed<sup>21-23</sup> that the uric acid concentration of the serum is increased in this type of arthritis and that the pathologic changes observed are the result of the deposition of monosodium urate.<sup>21</sup> Although there is considerable evidence favoring the view that gout is a metabolic disease, its exact nature is unknown. Recurrent attacks of acute arthritis with complete freedom from joint symptoms in the intervals are characteristic of the disease. The time between the first and second attacks is variable. It may be months or years, the average time being eighteen months. The interval between attacks tends to decrease with each subsequent attack until chronic joint deformity becomes evident. The treatment of patients with gouty arthritis raises many questions. How should one treat the acute attacks? What treatment should be prescribed during the intervals of freedom? Can chronic gouty arthritis be prevented, and if not, how should it be treated? Does therapy influence the hyperuricemia? Are acute attacks preventable? Can one materially alter the course of the disease? Should one restrict the intake of purine, and if so to what extent and when?

The proper treatment of acute gouty arthritis is very gratifying to both patient and physician. Colchicine, if correctly administered, is practically a specific form of therapy for the acute attacks. We have never seen it fail to give relief. It should always be given in the crystalline form because the potency of the wine or tincture of colchicine is extremely variable. We prescribe 1/120 gr every one or two hours until relief from pain is obtained or until diarrhea, nausea, or vomiting appears. From eight to sixteen doses usually suffice, but occasionally more are necessary. The drug is then discontinued. Freedom from pain and subsidence of swelling occur within twenty-four to seventy-two hours. The diarrhea is usually sufficiently severe to require treatment with

paregoric, 4 cc. is given for each loose bowel movement until the diarrhea is checked. Once the patient has established the amount necessary to produce such symptoms, he can reduce the total dose by one or two pills or granules and still obtain the desired effect without experiencing severe gastrointestinal symptoms. We have never observed any other untoward effects. Hypersensitivity to the drug is unknown, nor does it lose its efficacy with repeated administration. The patient should always carry colchicine with him. The appearance of any of the usual prodromes<sup>22-24</sup> calls for immediate institution of colchicine therapy. If the patient always follows these rules, many prolonged and incapacitating attacks may be prevented.

Absolute bed rest is always indicated during the attacks, particularly when weight-bearing joints are involved. Avoidance of even normal joint use prevents recurrent minor traumas and thereby shortens the attack. Premature resumption of normal activity may precipitate another attack. Occasionally opiates are necessary until the full effect of the colchicine has been obtained. Hot compresses or packs every three hours may be helpful. Moist heat is always preferable to dry. An occasional patient insists that cold gives more relief than any form of heat. We never employ cinchophen because of the attendant risks and the fact that the colchicine when administered properly is more efficacious. The only other measures we employ for acute gouty arthritis are an increased fluid intake and the avoidance of the few foods with a high purine content. No one has ever proved that an acute attack is materially shortened by a diet free of or low in purine content.<sup>23</sup>

Certain workers<sup>24</sup> contend, without presenting the necessary proof, that adherence to a rigorous regime during the symptomless periods will reduce the number of subsequent attacks and sufficiently alter the course of the disease to prevent chronic gouty arthritis. We cannot agree with such claims. Evaluation of the effect of therapy on the course of a disease as variable from patient to patient as is gout is extremely difficult. Those who think the course of gout can be altered believe that carbohydrates and proteins promote urate excretion and that fat inhibits it, and therefore prescribe a diet low in purine (100 to 150 mg. as compared with the normal intake of 600 to 1000 mg.) and fat, high in carbohydrate and protein. A high-protein, low-purine diet of this type is possible if one gives generously of such protein foods as milk, cheese and eggs. Until proof is forthcoming that this type of dietary favorably influences the hyperuricemia and the clinical course

of gout, its prescription is hardly justified. It is a monotonous diet to which few people will adhere. In addition, it favors a deficiency of certain proteins, iron and vitamin B. We prescribe a diet of moderate purine content. This is readily accomplished by omitting with some regularity the few foods with a high purine content.\* Absolute restriction of alcohol is frequently advocated without adequate proof that such abstinence is therapeutically beneficial. If small amounts of alcohol are allowed, whisky is probably preferable.

Some writers<sup>24</sup> believe that cinchophen in 7½-gr doses three or four times a day, three or four days out of each week, will aid in controlling the symptoms and hyperuricemia of gout. Such therapy may be symptomatically effective but does not reduce the hyperuricemia, and it may be harmful.<sup>23</sup> Furthermore, sodium salicylate in doses of 60 to 100 gr. a day, three or four days out of each week, will result in an equally great urate diuresis as that which occurs with cinchophen. Therefore, we prefer the repeated administration of salicylates. Thiamin chloride and glycine administration are not beneficial.

A fluid intake of 3000 to 4000 cc. a day should be encouraged in order to maintain a high urinary output. The latter may allow for an increased urinary urate excretion and will protect the kidney against uric acid stone formation. However, this is best accomplished by keeping the urine alkaline through the administration of three or four teaspoonfuls of sodium citrate each day. The patient himself can make a reasonably accurate urine pH determination by using nitrazine paper.

The gouty patient should be warned that trauma, major or minor, physical or physiologic, and other provocative factors may precipitate an acute attack of gouty arthritis.<sup>23, 24</sup> Major operative procedures may do the same.<sup>24</sup>

Chronic gouty arthritis and its complications are difficult to treat. Colchicine, 1/120 gr. three times a day, may be helpful. Regular rations of salicylates are often necessary. Orthopedic measures, including physiotherapeutic procedures, joint aspirations, immobilization, correction of deformities by casts or operative interference and so forth may be indicated. Troublesome tophi can be excised with safety. Excellent foot care should always be provided.

#### HEMOPHILIC ARTHRITIS

Arthritis is one of the commonest manifestations of hemophilia. It may present itself in one of two forms: acute hemarthrosis, the result of a single intra-articular hemorrhage, and the chronic

\*These include anchovies, beef, brain, gravies, kidneys, liver, meat extracts, sardines and sweetbreads.

form, which is usually the result of repeated intra articular bleeding. Permanent reduction of the increased clotting time is the only type of treatment that would prevent and control hemophilic arthritis. To date, no such therapy is known. Treatment of the acute hemarthrosis should consist of rest and immobilization with a splint or plaster cast until the bleeding stops and the acute inflammation has subsided. If the pain caused by the sudden intra articular distention is severe, cautious aspiration with a small-bore needle may be undertaken, but under no circumstances should aspiration be performed until the clotting time has been reduced by means of transfusion. This method of treatment allows for a more rapid subsidence of the signs and symptoms. During the stage of recovery, mild, active exercise and massage are permitted. In the chronic form correction of deformities may be accomplished by slow traction or other gradual and gentle methods of improving position and gaining motion. Walking calipers and braces may be helpful if weight bearing joints are involved. Under no circumstances should the joints be strenuously manipulated or opened.

#### ANAPHYLACTIC ARTHRITIS

The arthritis of serum sickness is the only type of arthritis that can be classified as anaphylactic or allergic in nature. Its recognition is never difficult. It is a self-limited disease which clears completely, leaving no residual signs. The treatment of this type of arthritis is entirely symptomatic. Analgesics, usually one of the salicylates, are indicated. Heat is often helpful. Hypnotics are occasionally required. Epinephrine, if helpful at all, should be used at the onset of the complication. Further trial of the use of histamine in both the prevention and treatment of serum sickness is necessary before concluding that it is of value for this type of arthritis.

#### ARTHRITIS AS A MANIFESTATION OF OTHER DISEASES

There is no known specific therapy for the articular manifestations of erythema nodosum, acute disseminated lupus erythematosus, purpura and

pulmonary osteoarthropathy. In some cases symptomatic measures such as heat, analgesics, opiates and splinting are necessary and beneficial.

The term "psychosomatic rheumatism" is employed to designate the ill-defined skeletal aches and pains experienced by the psychoneurotic individual. Psychotherapy is indicated in such cases, but a definite statement of its results must await further study.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 26341

#### PRESENTATION OF CASE

A sixty-year-old American taxicab driver was admitted to the hospital complaining of severe headaches.

The patient was in his usual vigorous health until six months before entry when he was stricken, while driving his cab, with a headache which became increasingly severe, necessitating his going home. The headache was located over the left eye and in the region of the occiput, whence it radiated down the neck. It persisted almost continuously until the time of admission. He noted that coughing, stooping and straining at stool aggravated the pain, which was only temporarily relieved with medicaments prescribed by two or three local physicians. Four months before entry occasional diplopia with blurring and dimness of vision had occurred, and had persisted intermittently. He stopped work three months before entry in an unsuccessful attempt to obtain relief from his symptoms by rest. During the month before admission he vomited precipitously three or four times after eating, he noted frequent faint spells, and ten days before entry he fell, struck his head and was unconscious for a few minutes. He had lost 25 pounds in weight during his illness, had experienced an impairment in memory and, at times, had noted dyspnea and orthopnea, with nocturia two to three times.

The marital and family histories were essentially negative. He had had scarlet fever at the age of twelve, without known complications.

Physical examination revealed a well-developed and well-nourished but drowsy and mentally clouded man complaining of severe headache. The fundi showed cotton-wool exudates with flame-shaped perimacular hemorrhages, especially on the left. The external ocular movements were normal. The ears, nose, mouth and throat were essentially normal. The apex of the heart was percussed at the midclavicular line in the fifth interspace, the sounds were loud, the rhythm regular, and the aortic second sound loud and snapping. The blood pressure was 195 systolic, 140 diastolic. The lungs were normal. The abdominal, rectal and neurological examinations were negative.

The temperature, pulse and respirations were normal.

The blood showed a red-cell count of 5,200,000 with 72 per cent hemoglobin (Sahli), and a white cell count of 12,000 (later 18,000) with 80 per cent polymorphonuclears. A lumbar puncture showed normal dynamics. The spinal fluid had a total protein of 216 mg and a sugar of 62 mg per 100 cc. A blood Hinton test was negative. The blood nonprotein nitrogen was 36 mg per 100 cc., and a phenolsulfonephthalein test showed 5 per cent excretion in fifteen minutes, with 25 per cent excretion at the end of six hours (the patient had been unable to void at the proper time). The visual fields were normal except for bilateral enlargement of the blind spots. X-ray examination of the chest revealed a heart slightly enlarged in the region of the left ventricle. The aorta was markedly elongated and tortuous, with some generalized dilatation and slight calcification. The lung fields were clear.

The temperature, pulse and respirations remained normal for five days, and he was apparently getting along well. On the sixth day at 8 p.m. he complained of a sudden severe bilateral mid-back pain, which apparently radiated upward to the region of the neck and head. He perspired profusely. The pulse was strong and rapid, with a blood pressure of 242 systolic, 144 diastolic. He groaned, was disoriented and made statements that he would die that night. Paraldehyde and luminal were administered. He arose and, with assistance, "walked off" the pain in five minutes. There were no reflex changes. He complained of no pain for the remainder of the evening. The next morning he was stuporous, semicomatose and under the influence of paraldehyde. He did not respond to painful stimuli, but was able to move all his extremities. That afternoon he conversed with his wife, did not mention any pain and said he "felt fine." The temperature, pulse, respirations and blood pressure continued to rise as they had for the previous day. In the evening he became noisy and active, and then died. He continued to breathe three minutes after the heart had stopped beating.

#### DIFFERENTIAL DIAGNOSIS

DR. PAUL D. WHITE: This man's illness had a very abrupt onset; there was not a slowly increasing amount of headache. Something apparently happened acutely.

I shall discuss this case in two parts, because the second half of the illness, although indirectly related, is not a part of the first. Headaches, disturbance of vision, vomiting (not extreme or per

sistent), fainting spells and, on one occasion, a fall, when he was unconscious a few minutes, were the chief complaints. There was also loss of weight, with impairment of memory, dyspnea, orthopnea and nocturia. Such evidence of circulatory disturbance in the head with increased pressure might come from a variety of causes, including brain tumor, perhaps with hemorrhage into it to explain the sudden onset of symptoms. However, as we go on down the list of symptoms to the findings on examination we note hypertension and we know that hypertensive encephalopathy can almost exactly mimic increased intracranial pressure due to tumor, especially when the hypertension enters the malignant phase. I do not believe that we can explain the situation wholly by the gradual development of increasing intracranial pressure. There may have been increasing pressure from edema, but the very beginning was sudden and that does suggest a definite vascular lesion, either a hemorrhage, an expanding small aneurysm or an infarct, or, as I said there may have been a tumor with hemorrhage. It is not likely that an abscess could explain the situation with so long a story and without fever. Usually there are increased spinal-fluid pressure and superimposed cerebral edema with such small or large cerebrovascular lesions, and cerebral arteriosclerosis is always present in this group of cases. Hypertensive encephalopathy is more likely than is brain tumor. At the end of the first paragraph there is a little evidence of coronary and renal involvement, associated with the hypertension. The eyeground changes are characteristic of severe hypertensive retinopathy. Physical examination revealed no evidence of cardiac enlargement, but x-ray examination did show slight increase in the size of the left ventricle, as we should expect. It is quite likely that some hypertrophy of the heart was found, without much dilatation and with little or no evidence of failure, despite the history of dyspnea and orthopnea. Some renal vascular involvement was almost certainly discovered.

Certain intracranial tumors have been associated with hypertension, especially Cushing's syndrome (basophilic adenoma of the pituitary gland), but the other characteristics of Cushing's syndrome are not present, and we need not consider that further. The spinal fluid findings I do not believe are diagnostic. Inflammatory changes, degenerative changes or tumor could each account for the increased protein, and exudation of serum around a small hemorrhage could account for some. We might have a comment on that point later by Dr. Kubik.

Apparently there was no uremia although renal involvement was evident.

Thus I believe that a severe grade of hypertension, without any past history indicating a nephritis as a background and without the certainty of any other complication such as a tumor, was the explanation of the findings in the first part of the record.

The thing that killed him is, I think, related to the hypertension. It began with sudden severe transitory mid back pain radiating upward, not downward as pain from the kidney would do. There is no statement about radiation to the front of the chest. We have just seen, at medical grand rounds, an unusual case of coronary thrombosis, with pain starting in the back but radiating to the front of the chest. In the present case the pain remained in the back, certainly that would be an unusual story for a coronary thrombosis that occurred as a fatal complication of hypertension.

Terminally the systolic pressure was considerably higher than it was at the previous reading; the diastolic pressure was about the same.

We have all become schooled here in the past few years to the idea that sudden severe pain in the back in hypertensive patients may be due to a dissecting aortic aneurysm, and that seems to be the probable diagnosis in the present case, even though the condition is rare, and even though this description fits it almost too well. Pulmonary embolism or another complication of that sort is not so likely. The episode that caused the pain in the back can be explained by final rupture of the aorta into the pleura, mediastinum or elsewhere. I think then that I shall follow what I believe is a conservative course, and diagnose this case as malignant hypertensive disease with some involvement of the heart and kidneys therefrom and with marked involvement of the brain including a good deal of cerebral scarring and vascular disease and perhaps infarction or even a small aneurysm that has increased in size, not on a syphilitic basis, and aortic disease with dissection of the aortic wall, aneurysm and rupture.

DR. TRACY B. MALLORY. Assuming that the death was due to dissecting aneurysm. Dr. White, how would you explain the fact that he did not develop paralysis of the legs, which is usual?

DR. WHITE. One case I remember very well—the first one we analyzed correctly—was diagnosed despite the fact that we felt a good pulse in both feet; that finding, however, was one of the things that made us hesitate to make the diagnosis. There was a rupture of the dissected wall

into one of the iliac arteries, which had prevented the compression and occlusion of those vessels. Such might have occurred in this case.

DR BERNARD M JACOBSON The diagnosis of the medical service up to the day of death was that given by Dr White—hypertension with cerebral involvement. We saw him the morning after the episode of pain and were very much impressed by the fact that the patient was irrational and stuporous and somewhat under the influence of paraldehyde. The cerebral symptoms were so marked the evening before and the pain was so transitory that we believed he had been suffering from a cerebral vascular accident, probably hemorrhage. The lungs that morning were entirely filled with rales, and surprisingly enough, the pulse was very firm and the blood pressure higher than it had been the day before. My guess at that time was that he had a diffuse bronchopneumonia and the day before had had a cerebrovascular accident.

#### CLINICAL DIAGNOSES

Malignant hypertension with hypertensive encephalopathy

Retinitis

Nephrosclerosis

#### DR WHITE'S DIAGNOSES

Hypertensive cardiovascular disease (malignant phase)

Hypertensive encephalopathy with multiple vascular lesions

Left ventricular cardiac hypertrophy

Vascular nephritis

Dissecting aneurysm of the aorta with rupture into iliac artery or external rupture with fatal hemorrhage

#### ANATOMICAL DIAGNOSES

Dissecting aneurysm of the aorta extending into the superior mesenteric, renal and common iliac arteries, with rupture into the pericardium

Hemopericardium

Cardiac hypertrophy, hypertensive type

Pulmonary congestion with slight edema

Arteriosclerosis of coronary arteries, aorta and cerebral arteries, minimal

Infarction of pons

Nephritis, chronic vascular

#### PATHOLOGICAL DISCUSSION

DR MALLORY We found in this man an extensive dissection of the entire aorta. The rupture through the intima had occurred at the mouth

of the innominate artery, and dissection had spread both upward as far as the annulus of the aortic valve and downward as far as the iliac arteries. Throughout the entire course of the aorta the wall was split into two complete layers separated by clotted and fluid blood. In the lower abdominal aorta, 7 cm below the inferior mesenteric artery, a second intimal rupture had occurred, through which the current of blood was able to escape back into the original lumen, therefore there was no shutting off of the circulation in the legs. The dissection had extended a few millimeters to centimeters down a number of the small and large branches of the aorta. The mesenteric arteries and the renal arteries, for example, showed dissections 2 or 3 cm in length. As in most cases of dissecting aneurysm the outer layer eventually gave way and hemorrhage occurred. In this case it was into the pericardium, and the presence there of 700 cc of blood is enough to warrant the presumption that he died of cardiac tamponade. The other findings in this case, I think, are to be grouped together as those characteristic of hypertension. The heart was hypertrophied, particularly the left ventricle.

DR WHITE How much did it weigh?

DR MALLORY Five hundred grams. The kidneys were distinctly smaller than normal—250 gm—and showed the characteristic appearance of so-called "malignant vascular nephritis." The brain showed a few lesions which Dr Kubik will describe.

DR CHARLES S KUBIK It is curious that we find so little at autopsy to explain the cerebral symptoms in these hypertensive cases. In many of them, as Dr White said, the spinal-fluid pressure is elevated, but in others with severe head aches the pressure may be normal. The total protein of the spinal fluid is often elevated up to 70 or 80 mg per 100 cc, usually some figure less than 100 mg. I do not know of any other case in which the total protein has been over 200 mg, as it was here. A number of tiny hemorrhages were present in the pons, cerebral cortex and subcortical white matter. All of them were less than 1 mm in diameter, some scarcely larger than a pinpoint. They varied in color, thus indicating that some were older than others. Sections showed so-called "ring hemorrhages" surrounding thrombosed arterioles and small arteries. One hemorrhage, a little larger than the rest, situated on the surface and involving the subarachnoid space, may possibly have been responsible for the first headache, which had a sudden onset and was particularly severe. There were also small infarcts in the pons and in the basal ganglia, the largest

one measuring less than 0.5 cm in diameter. There are many things about these cases that I do not understand. In some of them where a high spinal-fluid pressure had been recorded during life we have not found any evidence of increased intracranial pressure at autopsy. The explanation may be a temporary circulatory disturbance which had subsided before death.

### CASE 26342

#### PRESENTATION OF CASE

A sixty-five-year-old widow was admitted in coma.

The patient was apparently well until six years before entry, when she began to note dyspnea on climbing stairs, and persistent ankle edema. She consulted her physician who diagnosed "leaky heart valves," but offered no treatment. Her complaints subsided somewhat following this episode, and she was fairly well until two years before admission, when jaundice and weakness appeared. She was told by another physician that she had a severe blood disease, and was then treated with injections three times a week for a long time. Tiring of this the patient lapsed in her treatment, but as her symptoms returned she again consulted her physician, who informed her that her disease had progressed far and that she would have to eat half a pound of raw liver every day. This regimen was too rigid for her, and she remained on it for only six months.

Several months before entry she developed nervousness, prominent eyes and a ravenous appetite, but in spite of the latter she lost 30 pounds in weight, dropping from 190 to 160 pounds. The patient became progressively weaker, and one week prior to hospitalization went to bed. She became so weak and clouded mentally that she failed to recognize her family. Although she had no pain, her physician had injected morphine about twenty-four hours before admission. Thirty minutes later she became unconscious, and remained in a stupor from which she could not be aroused.

The family, marital and past histories were non-contributory.

Physical examination revealed a well-developed, obese, moderately icteric woman in coma whose breathing was slightly stertorous. The skin was dry, and the mucous membranes pale. There was a marked exophthalmos, with chemosis and icteric scleras. The retinal vessels were moderately sclerotic, with two small hemorrhages on the right. The disks were flat. The pupils reacted slightly to light. The thyroid gland was

not remarkable. The lungs were clear throughout. A coarse systolic murmur was heard over the whole precordium. The rhythm of the heart was regular, the aortic second sound was greater than in the pulmonic. The liver edge was palpated a handbreadth below the costal margin, and that of the spleen was noted two fingerbreadths below. There was slight non-pitting edema of the lower extremities. All the reflexes were normal, equal and active, except for the plantars which were equivocal.

The temperature was 99°F, the pulse 110, and the respirations 20.

Laboratory examination revealed a negative urine except for a ++ bile test. The blood showed a red-cell count of 1,420,000 with 36 per cent hemoglobin (Sahli), a hematocrit of 18 per cent, a color index of 1.2, a mean corpuscular volume of 126 cu microns and a reticulocyte count of 6 per cent. There was a white-cell count of 21,000. A differential count showed 25 per cent polymorphonuclears, 5 per cent lymphocytes, 2 per cent monocytes, 2 per cent eosinophils, 15 per cent myelocytes, 4 per cent megaloblasts, 16 per cent erythroblasts and 31 per cent normoblasts. The stools were guaiac negative. A blood Hinton test was negative. Lumbar puncture revealed normal dynamics, with a xanthochromic fluid and 400 and 280 red blood cells per cubic millimeter in the first and second tubes respectively, the ammonium sulfate ring test was positive. The blood nonprotein nitrogen was 66 mg per 100 cc., and the chlorides were equivalent to 116 cc. N/10 sodium chloride. The carbon-dioxide combining power was 56.2 vol per cent, a van den Bergh test was unsatisfactory.

The patient was given three 500-cc. transfusions, parenteral fluids with glucose, tube feedings, intramuscular liver and vitamin B<sub>1</sub>. The temperature rose to 101°F on the second and third hospital days, the pulse ranged around 90, and the respirations varied between 20 and 25. She became less active and developed rales throughout the right chest posteriorly. Respirations became labored, with dilatation of the nasal alae. Purulent sputum appeared in the throat, without expectoration. She rapidly failed and died on the second hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR. ALFRED KRANES. As is the case with many patients admitted in coma there are many gaps in the history which one would like to have filled in but which friends and relatives of a patient frequently cannot supply. One would like to know for example, whether the jaundice which



had been noted two years before admission had been constant or intermittent, whether it was associated with any changes in the color of the urine or stools and whether there had been any pain. It would also be of considerable value to know whether the injections, which presumably consisted of liver extract, had resulted in any improvement. The fact that she discontinued treatment might mean either that she had recovered sufficiently so that she felt it was no longer necessary or that she had become discouraged over the failure to improve. Because of the statement that she again consulted her physician when her symptoms returned, we might infer, however, that she actually did improve. It would also be of considerable help to know whether the half pound of raw liver a day for six months resulted in any improvement.

I do not quite know how to evaluate the nervous symptoms which developed prior to admission. The description sounds a good deal like the picture of thyrotoxicosis, but certainly that cannot be the whole story. If she did develop thyrotoxicosis, it must have been in addition to whatever preceded it. One would also like to know whether there were any paresthesias of the extremities.

So far as the physical examination goes, there is evidence of enlargement of both the liver and spleen, although I must add here that the liver being palpable a handbreadth below the costal margin does not necessarily mean it will be increased in size post mortem. All too frequently the clinical and pathological size of the liver do not agree, as has so often been pointed out in these exercises. The presence of marked exophthalmos seems to confirm the thyrotoxic symptoms as given in the history.

The laboratory tests are extremely helpful. The blood examination indicates the definite presence of a hyperchromic macrocytic anemia that was quite typical of pernicious anemia except for the white-cell count and smear. An elevated white-cell count is not usually seen with pernicious anemia, but it may occur in the presence of an acute infection, in this case the elevation may be more apparent than real because the count probably included an enumeration of the many nucleated red cells which were found.

So far as the lumbar puncture goes, one cannot be certain from the data here whether or not there had been a subarachnoid hemorrhage. The xanthochromic fluid may merely have been the result of prolonged jaundice and the red cells may have been traumatic, particularly since the number diminished in the second tube. I do not be-

lieve we can attach too much importance to the elevated nonprotein nitrogen since the blood sample was taken the day before death. There seems to have been no other indication of renal damage. The urine is stated to have been normal, although no specific gravity is mentioned.

As for the differential diagnosis, the patient apparently had a chronic disease which had been going on for six years with remissions and which probably responded, at least on one occasion, to parenteral liver injections. In addition the blood examination reveals the presence of a hyperchromic macrocytic anemia which was quite consistent with pernicious anemia. We have the additional information that it was megaloblastic. I do not see, therefore, how we can escape the diagnosis of pernicious anemia. The presence of jaundice and a severe anemia always raises the question in a patient of this age of an acquired hemolytic anemia, which would seem to be excluded by the large diameter of the red cells, by the absence of a marked reticulocytosis and by the finding of bile in the urine.

The diagnosis of pernicious anemia is of course consistent with the presence of chronic icterus, but there are certain features here which point in addition toward an intrinsic disease of the liver as the cause of the icterus. In the first place, the excretion of bile in the urine is very unusual in uncomplicated pernicious anemia. Nor is it usual to have the liver enlarged as much as appears to have been the case here. Another fact which points toward diffuse liver disease is the apparent remarkable sensitivity to morphine. You will remember that she went into coma shortly after an injection of morphine, from which she never recovered. There are two diseases in which this sensitivity occurs. One is myxedema, the other is diffuse liver damage, usually cirrhosis. There certainly is no evidence of myxedema in this case, and we do have evidence pointing toward liver disease. On the basis, therefore, of chronic jaundice, urobilinuria, enlarged liver and spleen and sensitivity to morphine, I am inclined to think that she did have a cirrhosis of the liver, just what type of cirrhosis I should not venture to guess.

The presence of a macrocytic anemia has frequently been described in association with liver disease, and I believe such is the case here. Many of these patients are resistant to liver therapy for some inexplicable reason. Of course, we do not know that this patient did not respond to liver since the history is very inadequate.

Whether or not she had thyrotoxicosis, I should not venture to state, since the evidence is too in-

conclusive. I think it would be foolhardy to make such a diagnosis in a patient who is admitted in coma and dies the next day. From the history and the exophthalmos, one might suspect its presence, but I do not believe we can go any farther than that. I shall, therefore, make diagnoses of cirrhosis of the liver of undetermined type, pernicious anemia and a terminal pulmonary infection, probably bronchopneumonia. There may also be some renal damage, which occasionally occurs in any jaundice of long standing—a so-called "bile nephrosis." We only have a single test of renal function taken the day before death—an elevated nonprotein nitrogen, which may mean nothing so far as anatomical damage to the kidney is concerned. We can go no farther than to mention this possibility.

#### CLINICAL DIAGNOSES

Pernicious anemia  
Bronchopneumonia

#### DR. KRANES'S DIAGNOSES

Cirrhosis of the liver, type undetermined  
Pernicious anemia.  
Terminal pulmonary infection (? bronchopneumonia)

#### ANATOMICAL DIAGNOSES

Pernicious anemia, relapse.  
Arteriosclerosis, generalized  
Extramedullary hematopoiesis liver and spleen.  
Nephritis, chronic, vascular, slight  
Jaundice, slight.  
Ascites, slight.  
Hydrothorax, slight, bilateral  
Leiomyoma, uterus.  
Cholelithiasis.  
Umbilical hernia  
Ovarian cyst

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY. The picture presented by this patient is one which some of the younger

of us have perhaps never seen and which the older of us are in some danger of forgetting. Death primarily from pernicious anemia has become a rarity and can only result from the grossest medical incompetence or from a suicidal lack of co-operation on the part of the patient. The picture seen in this patient at autopsy was one which was very familiar prior to 1925 but is rarely seen in a laboratory of pathology at the present time. The entire bone marrow was hyperplastic, including that in the central portions of the long bones. On microscopic examination it was evident that the marrow was composed predominantly of erythroblastic elements with a marked shift to the left and a predominance of megaloblasts. The next most numerous elements were large plasmacytes containing many phagocyte red cells. Phagocytosis of red cells is, however, in all probability a post mortem phenomenon, as the late Dr. Francis W. Peabody showed in his classic studies of the marrow in this disease. Both the liver and spleen were moderately enlarged and showed considerable erythropoiesis, more than is usually found in a fatal case of pernicious anemia. The liver, in addition, showed extensive central necrosis, which is a usual finding. All the reticuloendothelial system showed some degree of hemosiderosis, much less, however, than is often seen. The heart was considerably hypertrophied and showed on microscopic examination many small scattered foci of fibrosis, there did not appear to be enough coronary narrowing to explain this. The thyroid gland was enlarged and nodular, but sections showed no evidence of hyperplasia. It is within the limits of possibility that she may have had true hyperthyroidism in the past which had undergone spontaneous remission, leaving, however, a permanent exophthalmos and a hypertrophy of the heart. This, however, is only speculation. There was no subarachnoid hemorrhage, in fact, we could find nothing beyond mild arteriosclerosis in the brain. The patient evidently had an idiosyncrasy to morphine, but I do not believe that on anatomical grounds we can incriminate either the thyroid gland or the liver as responsible for it.

# The New England Journal of Medicine

Formerly the  
Boston Medical and Surgical Journal

Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND  
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE  
ON PUBLICATIONS

Official Organ of

THE MASSACHUSETTS MEDICAL SOCIETY  
THE NEW HAMPSHIRE MEDICAL SOCIETY  
THE VERMONT STATE MEDICAL SOCIETY

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SUBSCRIPTION TERMS \$6.00 per year in advance postage paid for the United States Canada \$7.82 Boston funds (including war-exchange tax) per year \$8.52 per year for all foreign countries belonging to the Postal Union

MATERIAL for early publication should be received not later than noon on Saturday

THE JOURNAL does not hold itself responsible for statements made by any contributor

COMMUNICATIONS should be addressed to the *New England Journal of Medicine* 8 Fenway Boston Massachusetts

## MEDICAL PREPAREDNESS THE LISTING OF THOSE CONCERNED WITH MEDICAL CARE

THE second problem of medical preparedness has to do with the accurate listing of those who are qualified to participate in medical or public-health service. Such a list should include the names of physicians, dentists, public-health officers, nurses and laboratory technicians, and should be supplemented by specific information regarding age, marital status, experience, specialized training, teaching, hospital or other positions, and so forth. Only with the latter data on hand can intelligent choice of those best suited for the various types of service be made. Sufficient personnel must be left in all parts of the nation to provide adequate medical care for the civilian population,

the staffs of medical, dental and nursing schools must not be so depleted that their teaching facilities are seriously impaired, and those who go into service must be assigned, so far as possible, to positions with responsibilities that, by training and experience, they are qualified to assume. During the rush that accompanied the mobilization of 4,000,000 men in 1917, these matters received scant attention, and the many mistakes that followed should and can be avoided.

The listing of the medical profession has already begun, the American Medical Association, through the Committee on Medical Preparedness, having forwarded questionnaires to every physician in the United States. When these have been filled out and returned all the data will be transferred to punch cards and, hence, be readily available. Furthermore, state and territorial chairmen on medical preparedness have been appointed, whose functions include contact with other state chairmen in their vicinities through the corps-area representative of the Committee on Medical Preparedness, the organization of state or territorial and county committees on medical preparedness, the promotion of civilian health, the dissemination of information to interested groups, the furnishing of additional data relative to the punch cards, the verification of the qualifications of physicians desired for service and the maintenance of adequate facilities for civilian medical care. In addition the Committee on Medical Defense adopted a resolution, a copy of which has been forwarded to various government officials in Washington, recommending that, in preparing for the conscription of personnel, provisions be made for the continuation of medical education and for the exemption of all medical students and interns in accredited and approved institutions.

All the necessary steps for the listing of physicians seem to have been taken. It remains for all physicians to fill out completely and correctly the questionnaire and to return it promptly, if they have not already done so. And it is to be hoped that information of a similar nature will be obtained from all groups, professional or otherwise, involved in medical and public-health services.

## DRUGSTORE PRESCRIBING

MUCH activity in public health proceeds with out penetrating the level of consciousness of practicing physicians. From time to time, they are made cognizant of this or that phase of public-health activity but often fail to maintain a continuing interest in this part of medicine. So long has the U S Public Health Service rendered important service to the country that its activities are apt to be taken for granted. This valuable governmental agency one is prone to associate with the old Hygienic Laboratory, now the National Institute of Health, and the various hospitals that it runs, and its co-operation with other agencies concerned with the health of the country are overlooked.

A recent activity of deep concern to all is the problem of venereal-disease quackery. The wide spread campaign inaugurated against syphilis by Surgeon General Parran makes one forget the toll of gonorrhea. Indeed, it may not be too exaggerated to state that the greatest advance in many centuries in the treatment of gonorrhea—the use of sulfanilamide—may prove to increase rather than decrease half-treated cases produced by quack and “counter prescribing.”

The trends in this direction are indicated clearly in the report\* of a study conducted by the American Social Hygiene Association, in co-operation with the U S Public Health Service. A nationwide survey of over a thousand drugstores in thirty-five cities, widely scattered, indicates the prevalence of drugstore prescribing and the sale of alleged remedies for self-diagnosed syphilis or gonorrhea. Approximately half the drugstores visited urged the patient to see a doctor but were willing to sell bottled remedies when asked for by name. Of thirty different preparations found to be generally available, only three or four contained substances recognized in the treatment of these diseases, the remainder being completely worthless mixtures. The cost of these remedies varied from one to three dollars a bottle for in-

redients costing a few cents and worth nothing to the purchaser.

In comparison with a similar survey made in 1933, there is a statistically significant increase in counter prescribing. Particularly pertinent is the fact that of the drugstores visited in 1933, about 30 per cent refused either to diagnose or to sell remedies without prescriptions, in 1939 only 7 per cent fell into this group. Advertising, on the whole, appears to have declined. In the 1933 survey it was pointed out that a total of nearly five million people believe themselves to have either gonorrhea or syphilis, whereas only two and a half million go to doctors for treatment.

The attack on this problem lies primarily in the suppression of the quack druggist, the continuing education of the ethical pharmacist through schools of pharmacy, pharmaceutical associations and trade and professional journals, and the eradication of the unethical medical practitioner. But the medical profession should help in the education of the laity, particularly in hospitals and clinics where poster advertising with slogans such as “Beware of Drugstore Prescribing!” might prove effective in spreading information among those classes most susceptible to this cruel type of charlatanism.

## MEDICAL EPONYM

### COURVOISIER'S LAW

The following translated quotation is taken from *Gannitsch statistische Beiträge zur Pathologie und Chirurgie der Gallenwege* [Critical and Statistical Contributions to the Pathology and Surgery of the Bile Ducts] (Leipzig F. C. W. Vogel, 1890) by Professor Ludwig G. Courvoisier (1843-1918), of Basle, Switzerland:

It is usually stated in reference books and textbooks that obstruction of the common bile duct leads to enlargement of the gall bladder by bile stasis. My experience is quite the opposite, and I am compelled to look on absence of distention in the presence of obstruction of the duct as characteristic of stone, and its presence as indicative of occlusion due to some other cause. If this observation should be further confirmed we should have here an important fact on which to base a differential diagnosis.

R. W. B.

\* Edwards, M. S. and Kline, P. M.: Illegal and unethical practices in the diagnosis and treatment of syphilis and gonorrhea. *Proc. Dis. I. form.* 21-19, 1940.

## MASSACHUSETTS MEDICAL SOCIETY

### STATE COMMITTEES ON MEDICAL PREPAREDNESS

Each state committee on medical preparedness, according to the plans advocated by the Committee on Medical Preparedness of the American Medical Association, is to consist of the president and secretary of the state medical society, the appointed chairman of the committee and the member or members of the Committee on Medical Preparedness within whose corps area the state is located and such other members as this group may select.

For Massachusetts this includes Dr Walter G Phippen, both as president and as First Corps Area representative of the Committee on Medical Preparedness, Dr Alexander S Begg, both as secretary and as appointed chairman, and Dr Stanley H Osborn, of Hartford, Connecticut, as the second First Corps Area representative of the Committee on Medical Preparedness.

The other state chairmen for New England are as follows

CONNECTICUT Dr George M Smith, Pine Orchard  
MAINE Dr John G Towne, Waterville  
NEW HAMPSHIRE Dr Deering G Smith, Nashua  
RHODE ISLAND Dr Halsey De Wolf, Providence  
VERMONT Dr Benjamin F Cook, Rutland

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

RAYMOND S TITUS, M.D., *Secretary*  
330 Dartmouth Street  
Boston

### PREGNANCY AND LABOR COMPLICATED BY PNEUMONIA

Mrs C H, a twenty-nine-year-old para II, was admitted to the hospital at 1 15 a m on March 6, 1939. She was not in labor, but complained of a headache, a cough and pains in the chest and shoulder. She stated she had had a severe chill lasting ten minutes just before being admitted to the hospital.

The family and past histories were not important. At the time of the previous delivery the patient was admitted with an upper-respiratory condition which was moderately severe, the temperature rose to 101°F and the pulse to 120.

The temperature on admission was 101.8°F, the pulse 120, and the respiration 25. Four hours later the temperature had risen to 103.8°F, the pulse to 140, and the respiration to 30. A medical con-

sultant was called, and the opinion was given that the patient had a definite early pneumonia. Physical findings showed dullness and impaired breath sounds over the left base and patches of consolidation on the right side. The white-cell count was 46,100. Cultures from the throat were taken. A chest plate was ordered. The x-ray report read, "There is mottled density at both bases, the upper lung fields are clear." An initial dose of 30 gr of sulfapyridine was given, and this was repeated in four hours, thereafter 15-gr doses were given at four-hour intervals.

The culture showed a Type 7 pneumococcus. In view of this finding, 100,000 units of Type 7 antipneumococcus serum was ordered. Skin and eye tests were negative, 20,000 units of serum was given at 7.30 p m, and since no reaction followed, the remaining 80,000 units was given at 9.30 p.m. Mild labor began about the time of the first injection of serum, the pains were of moderate intensity, and to ensure as much rest as possible 1/3 gr of Pantopon was given at intervals during labor. Labor continued uneventfully, with cough and general discomfort helped by Pantopon, until 5.30 a m, when the cervix was fully dilated and the membranes bulging. The membranes were immediately ruptured, and the head came down on the perineum. Under 1 per cent novocain infiltration, a small median episiotomy was made, and a male child, weighing 8 pounds, 8 ounces, was delivered. The baby cried spontaneously. The placenta and membranes were delivered intact, and the episiotomy wound was repaired with No. 0 chromic catgut.

The immediate condition after delivery was fairly good, with a pulse of 124 and a blood pressure of 100 systolic, 72 diastolic. At 8 a m, three and a half hours after delivery, the temperature had dropped to 97.2°F, the pulse to 88, and the respirations to 14. Sulfapyridine was omitted at this time, since the patient complained of nausea and itching over the upper chest. Codeine was given to control cough, and no other medication was ordered.

On the third postpartum day there was a good deal of pain on the left side, with diaphragmatic spasm. Patchy bronchial breathing could be heard, but in view of the normal chart it was believed that these areas would resolve. On the sixth postpartum day definite fluid on the left was noted, but no indication for paracentesis was found. X-ray examination confirmed the physical findings. The white-cell count at the time was 11,000, with the temperature about 99.5°F. Twelve days postpartum fluid could still be demonstrated but the temperature was normal and the patient felt well. Improvement continued in the subsequent week.

\*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

and the patient was discharged home well on the twenty-second postpartum day, with a healthy baby doing well on a formula

*Comment* The happy result in this case was undoubtedly due to the promptness of diagnosis and of treatment. Within twenty four hours after the initial chill the temperature was dropping, thirty-two hours after admission it was normal, and except for a slight rise from the fifth through the ninth day, due to fluid, remained there. Pan topon, in  $\frac{1}{2}$ -gr doses, gave the patient much comfort and aided in maintaining the best possible condition. Novocain infiltration worked extremely well, the episiotomy being repaired without incident. It seems quite remarkable that a patient can go through a definite pneumonia, be delivered and again have a normal temperature all within thirty six hours.

## COMMITTEE ON INDUSTRIAL HEALTH

The following cases represent situations which could arise at any time in industry. They are noteworthy in that they are preventable, yet they could occur and did occur in industries endeavoring to take all adequate steps in matters pertaining to the safety and health of employees

### METAL FUME FEVER

A forty-seven-year-old Irish-American who had been employed as a molder in a brass foundry for about twenty years, was seen by the company physician as the result of a telephone call from the man's wife. She stated that for some months previously her husband had come home every Monday night with a headache, which during the course of the evening developed into a severe shaking chill. The latter lasted approximately half an hour and was followed by a fever with very profuse sweating. By the next morning he was entirely normal and remained so until the following Monday evening. The patient was questioned in regard to these symptoms and freely admitted them. He stated that he had this difficulty only in the winter when closing the windows in the foundry decreased the natural ventilation. The situation had never bothered him so much as it did his wife, and he had not mentioned the matter to any physician, possibly because of some fear that he might lose his job.

In the course of this man's work he was required to pour molten brass into molds this operation lasting about ten minutes and being repeated four or five times a day. The alloy in question contained 5 per cent zinc. While pouring the molten metal he frequently had a small cloud of white fumes blowing directly into his face. Analysis of these fumes confirmed the presence of a considerable amount of zinc.

Further recurrence of this man's difficulty was entirely prevented by having him wear an approved respirator during the periods when he was engaged in pouring molten metal.

*Comment* This case is quoted as a typical story of metal fume fever known also as "brass chills" and "brass foundry ague." Characteristically one attack confers immunity on the individual so long as he continues re-

peated exposures to the fumes. This immunity is lost over a week end, holiday or vacation, and the individual becomes susceptible to another attack. Prevention of this condition consists of adequate ventilation or protection from the fumes by means of an approved respirator

### FUME INTOXICATION

A twenty-eight year-old American was employed painting the inside of a large steel casing. This was roughly in the shape of a huge bath tub completely open at the top and approximately 12 ft. long, 4 ft. wide and 5 ft. deep. He was applying with a brush a varnish in which the solvent was composed of equal parts of toluol and high flash naphtha. Working on the inside of this casing he naturally enough started painting at the top gradually working toward the bottom. After some little time he found that he was becoming extremely dizzy and was unable to climb out with considerable difficulty he attracted the attention of a nearby workman and was lifted out in a semiconscious condition. He was unable to walk unassisted and later stated that he had a pins-and-needles feeling all over his body. He struck one of the men who was assisting him, although he did not remember what produced this outburst of temper. He was taken immediately to the plant dispensary where he was found to be markedly cyanotic, with a respiratory rate of 10 and a pulse rate of 50. The skin was cold and clammy and he was still only semiconscious. Oxygen and carbon dioxide were administered by means of an H & H inhalator and complete recovery was very rapid. Less than an hour later he was taken home feeling perfectly well.

*Comment* This case undoubtedly represents acute intoxication by the fumes of a mixture of toluol and high-flash naphtha. It is here presented as a reminder that danger can easily be present even though a man is working in a location which would not ordinarily be regarded as an enclosed place. Here the entire top of the casing was wide open but the fumes of the solvent, being heavier than air, completely filled the lower portion of the casing in such concentration as to create an extremely hazardous condition. This case could easily have had a fatal outcome. The most satisfactory form of prevention in a situation of this sort consists either of adequate ventilation of the inside of the casing or of providing the employee with an air lined respirator. Precautions of this sort would automatically be employed if a man were being sent inside a closed tank. Care must be taken to see that similar conditions do not arise even though the area in question is not completely enclosed.

### TOOTH ETCHING

A battery repairman of one year's service reported at the clinic that he had been advised by his dentist that the enamel of his incisor teeth was being destroyed by the fumes present in the battery room.

Examination revealed that all buccal surfaces of the incisors not in contact with the lips during ordinary conversation presented an etched or ground-glass appearance. In fact, the cutting edge of these exposed teeth had been so eroded that the denture was exposed and had become darkened. Examination of this man's saliva revealed a pH of 6.1. A fellow employee with etched teeth showed a pH of 5.4 in the saliva.

About 20 per cent of the employees in the repair division were found to exhibit more or less etching of the incisor teeth.

Although these cases were not considered as industrial accidents by the insurance carrier an industrial accident

board awarded lump-sum payments for the porcelain jacketing of affected teeth

*Comment* A battery repair gang spends 30 to 40 per cent of a day in an atmosphere filled with droplets of sulfuric acid. This concentration of acid causes a choking and coughing for a few minutes in persons not accustomed to it.

Those men whose tooth enamel is affected by sulfuric acid seem to be either habitual mouth breathers or those with deficient or soft enamel structures. The habitual mouth breathers are affected because the acid deposited on the exposed teeth is not immediately diluted with saliva and thus tends to etch the enamel.

Personal communications with New England battery manufacturers and the Submarine Service of the U S Navy failed to reveal a similar situation with them. However, in the Middle West, industrial physicians have long been familiar with this condition.

Wearing of a filter mask, habitual nose breathing and the chewing of Oralgene Gum (containing magnesium oxide) have checked the incidence of tooth etching.

## DEATH

RENAUD—ULRIC J. RENAUD, M.D., of Brockton, died August 12. He was in his forty-fourth year.

Dr. Renaud received his degree from Bowdoin Medical School in 1919 and served his internship at Central Hospital, Lewiston, Maine. He was a member of the Massachusetts Medical Society and the American Medical Association.

Two daughters, his mother and father and a sister survive him.

## CORRESPONDENCE

### REGIONAL FRACTURE COMMITTEES

*To the Editor* The following remarks were delivered by me, as chairman, at the annual meeting of the regional fracture committees of the American College of Surgeons for each of the New England states. I believe that they may be of interest to your readers.

CHARLES L. SCUDDER, M.D.

374 Commonwealth Avenue,  
Boston.

\* \* \*

There are in the United States and Canada today about eighty regional fracture committees. Obviously, certain states and provinces have more than one committee. The aim of the General Fracture Committee, of which we here are a part, is to improve the treatment of fractures. You in this audience represent many communities throughout New England.

It is a generally recognized fact that surgeons have in times past been much more interested in pathological surgery than in purely traumatic surgery. Thus, the attention of surgeons and of general practitioners of medicine has not been focused on the recognition, treatment and end results of fractures. However, for over fifteen years, there has been developing in this country an increasing interest in fractures. With the rise in the incidence of fractures, with the increase in the complications attending fractures and with the occurrence of fractures and multiple injuries in rural districts, there has developed a definite demand for the services of medical men in caring for fractures.

It appears that many medical men are not only uninterested but unskilled and untrained in the treatment of these injuries. Moreover, many of these practitioners do not know that they are unable, or if they know, do not admit it, and unbelievably poor functional results follow

improper treatment. The causes of such lamentable unpreparedness on the part of the general practitioner are that in the medical school he had little or no instruction in the treatment of fractures and that since graduation he has not studied to perfect his treatment of these cases.

In order to improve the treatment of this increasingly important group of cases, there are three points of attack for us as members of the regional fracture committees: the undergraduate student, the practitioner of medicine, and the lay public.

There is at present a movement on the part of our educational committee to improve fracture instruction given in undergraduate medical schools in this country. Each of the seventy-eight medical schools is being approached by members of regional committees. Because of recent developments in the training of interns, residents and surgeons, it is becoming more and more evident that the medical school will never be able to deliver to the community a practitioner fitted to take care of fractures. Consequently, it is a part of our function as regional-committee members to insist that certain fundamentals be taught the medical student, and to help the practitioner to do those things in a fracture case which he can learn to do.

It is the aim of the members of the regional committees not only to perfect their own treatment of individual fractures but to see to it that every doctor in each rural community is taught to recognize a fracture when he meets it, to know when he cannot treat it, to understand how to transport safely such a victim of fracture to the nearest hospital where x-rays are available and films can be interpreted, and further, to realize the importance of immediately bringing the victim and a trained surgeon together.

The fact that here among ourselves exist differences of treatment of individual cases is reason enough for stressing first-aid and transport to a hospital where proper care can be given. The conditions in apparently similar fractures are so different that the treatment of fractures never should be standardized. However, first aid and transport may be and are standardized.

Difficulties in the making of a living for one's family and dependents are today more and more in evidence. Doctors are turning with avidity to traumatic surgery, but the vast majority of these men are without training or experience for such work. The public suffers, it is conscious of this mediocre treatment and rightly demands something better.

Through properly edited propaganda, lay people may come to learn that early recognition, painless transport, careful x-ray study and skilled treatment may be properly demanded by a person with a fracture. These same lay people may be instructed not to ask the surgeon for impossibilities. Because Neighbor Jones, following a fracture of the leg, walked a certain number of weeks afterward, is no reason why someone else with a broken leg should expect to walk as soon as he did. Professional criticism and impossible demands of ignorant laymen lead to suits for malpractice.

I am proud of the development of the regional fracture committees of New England. This joint assembly of the committees of these closely affiliated states offers a very helpful opportunity to improve our points of view.

We have listened to splendidly presented papers on special subjects, we have still others to hear this afternoon. It is appropriate that we should accommodate ourselves to recent advances in fracture treatment, but let us not forget that, as a member of a state committee, each committee man has a definite duty to perform toward the medical school, toward the general practitioner and toward the public.

The approved modern hospital is the workshop of such-

use medicine and surgery. All of you are attached to such hospitals and it is through these hospital workshops that our best results may be expected. I cannot hope to tell you how to deal with your own special problems. That is the business of the state chairman to work out in conference with his secretary and others. Let each state committee help the practitioner in the presence of a fracture, to avoid additional trauma and to hasten by proper transport, the contact of patient and trained surgeon.

If I were asked to name a great improvement in fracture treatment, I should reply the recognition of the importance of first-aid and transport, that is the preparation of the patient for proper surgery.

## NOTICES

### SUFFOLK CENSORS' MEETING

The censors of the Suffolk District Medical Society will meet for the examination of candidates at the Boston Medical Library 8 Fenway, Boston, on Thursday November 7 at 4:00 p.m.

Candidates should make personal application to the secretary and present their medical diplomas at least six weeks before examination (if graduates of foreign medical schools or schools not on the list recognized by the Council, at least eight weeks before).

### CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	ORTHOPEDIC CONSULTANT
Salem	September 3	Harold C. Bean
Haverhill	September 4	William T. Green
Lowell	September 6	Albert H. Brewster
Gardner	September 10	Mark H. Rogers
Brockton	September 12	George W. Van Garder
Pittsfield	September 16	Francis A. Slowick
Northampton	September 18	Garry deN. Hough, Jr.
Worcester	September 20	John W. O'Meara
Fall River	September 23	Eugene A. McCarthy
Hyannis	September 24	Paul L. Norton

### MASSACHUSETTS DEPARTMENT OF CIVIL SERVICE AND REGISTRATION

School Physician \$550 a Year Revere

Director of State Civil Service, Ulysses J. Lupien, has recently announced that a competitive examination is to be held on September 28 in order to find eligibles for appointment to the position of school physician School Department, Revere.

The entrance requirements are as follows: applicants must be registered physicians under the State Board of Registration in Medicine. The subjects and weights of the examination are as follows: training and experience, 2 practical questions, 3 total 5. Applicants must obtain a grade of 70 per cent in each subject in order to become eligible. The last date for filing applications is Saturday September 14 at 12 o'clock noon.

### CLINICAL CONGRESS OF THE CONNECTICUT STATE MEDICAL SOCIETY

The Clinical Congress of the Connecticut State Medical Society will be held at the Sterling Law Buildings, New

Haven on September 17, 18 and 19. Morning and afternoon sessions, beginning at 9:30 a.m. and 2:30 p.m. respectively will take place on the three days. Papers will be presented by well-known specialists in their fields.

The special subjects for the three-day afternoon courses will be hematology, fracture treatment and recent advances in the therapeutics of gastrointestinal disease.

Full information may be obtained by writing to the Connecticut Clinical Congress, 258 Church Street, New Haven, Connecticut.

### NEW ENGLAND SOCIETY OF ANESTHESIOLOGY

There will be a meeting of the New England Society of Anesthesiology at the Boston City Hospital on Monday September 16 at 8:00 p.m. Dr. P. D. Woodbridge will speak on the subject "Cyclopropane: Recent advances in precautions and usage."

### 1940 GRADUATE FORTNIGHT

The 1940 Graduate Fortnight of the New York Academy of Medicine will be held from October 14 to 25. The purpose of this meeting is to make a complete study and authoritative presentation of a subject of outstanding importance in the practice of medicine and surgery. The current topic is "Infections."

There will be a carefully integrated program, which will include morning panel discussions, afternoon clinics and clinical demonstrations at many of the hospitals of New York City, evening addresses and appropriate exhibits. The evening sessions at the Academy will be addressed by recognized authorities in their special fields, drawn from leading medical centers of the United States. The comprehensive exhibit will include books and roentgenograms, pathologic and research material and clinical and laboratory diagnostic and therapeutic methods. It is also planned to provide demonstrations of exhibits.

The following subjects will be included: experimental basis of chemotherapy in the treatment of bacterial infections; clinical bacterial chemotherapy results obtained and dangers encountered; a general consideration of bacterial infections; recent advances in knowledge of streptococcal infections; infections of the mouth, pharynx and upper respiratory tract; infections of the middle ear and nasal sinuses; infections of the teeth and surrounding structures; influenza; pneumococcal infections; bacterial meningitis; infections of the urinary tract; gonococcal infections in the male; gonococcal infections in the female; osteomyelitis and pyogenic infections of the joints; wound infections; puerperal infections; treatment of infections by methods other than chemotherapy; virus infections; acute poliomyelitis; brucellosis—undulant fever; rickettsial diseases; lymphogranuloma venereum; epidemic encephalitis; other forms of encephalitis and choriomeningitis and exanthematous diseases.

The Academy provides this program for the fundamental purpose of medical education; consequently all members of the medical profession are eligible for registration. A complete program and registration blank may be secured by addressing Dr. Mahlon Ashford, New York Academy of Medicine, 2 East 103d Street, New York City.

### SOCIETY MEETINGS AND CONFERENCES

SEPTEMBER 2-6—American Congress of Physical Therapy. Page 842. Issue of May 16.

SEPTEMBER 12-14—Foster-Peterson Association of Physicians. Page 263. Issue of August 15.

SEPTEMBER 16—New England Society of Anesthesiology. Note above.

SEPTEMBER 16-20—American Occupational Therapy Association. Page 263. Issue of August 15.



SEPTEMBER 17-19 — Clinical Congress of the Connecticut State Medical Society Page 305

OCTOBER 6-11 — Annual meeting of the American Academy of Ophthalmology and Otolaryngology Page 81 issue of July 11

OCTOBER 8-11 — American Public Health Association Page 655 Issue of April 11

OCTOBER 11-12 — Pan American Congress of Ophthalmology Page 898 issue of May 23

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OCTOBER 21 — American Board of Internal Medicine Page 369 issue of February 29

JANUARY 4 1941 — American Board of Obstetrics and Gynecology Page 1064 issue of June 20

MARCH 8 — American Board of Ophthalmology Page 201 issue of August 1

APRIL 21-25 — American College of Physicians Page 1065 issue of June 20

## DISTRICT MEDICAL SOCIETY

### SUFFOLK

NOVEMBER 7 — Censors meeting Page 305

## BOOK REVIEWS

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The statistical studies of environmental factors in the production of mental disease are very difficult to evaluate, since there are no control statistics. Furthermore, many environmental factors are not suitable for statistical study. For instance, such a simple factor as whether patients liked or disliked one or both parents is not capable of statistical treatment. In general this study shows a preponderance of environmental factors such as one would expect in the homes of people with "shut in" personalities, for instance, parents who avoided social contacts. Severe mental stresses resulting from financial difficulties, worries over sickness or death in the family, sexual difficulties or severe disappointments had been frequently imposed on the patients just prior to the mental breakdown. If these immediately precipitating factors are of importance there is no difference in their character or incidence in the manic-depressive group, as compared with that in the dementia praecox group.

Many case histories illustrating the occurrence of mental disease in the presence or absence of discernible hereditary or environmental factors are included in the volume leading to the conclusions that there are probably all degrees of predisposition to these diseases and that the interplay of environment on predisposition probably determines the appearance or absence of overt mental disease.

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# The New England Journal of Medicine

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VOLUME 223

AUGUST 29, 1940

NUMBER 9

## PELLAGRA IN THE AVERAGE POPULATION OF THE NORTHERN STATES\*

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WILLIAM D. ROBINSON, M.D. §

ANN ARBOR, MICHIGAN

PELLAGRA is not confined to those two groups, alcoholic addicts and the Southern poor, whose dietary habits are notoriously bad and among whom the severe manifestations of the disease are especially common. Lesser deficiencies, not accompanied by florid dermatitis, diarrhea or dementia, are common in the average Northern population. They are the cause of important impairment of health.

Many have commented on the decreased vitamin content of the modern American diet, due to an increasing consumption of sugar and refined flour, with an ensuing decreased consumption of vitamin-containing foods. Studies by members of the U. S. Public Health Service<sup>1</sup> have not shown good pellagra preventing values for many common foods other than meat, fowl and fish. The Bourquin-Sherman assay for vitamin B<sub>3</sub> is not a good indication of the pellagra preventing value of foods. It is, rather, a measure of the riboflavin content.

There is considerable individual variation in the vitamin requirements of highly standardized rats. Our observations indicate that some human subjects have unusual requirements without apparent organic cause. Many of our patients have had access to but have not selected an adequate diet. Many have had the onset of their deficiency symptoms during conditions which interfere with a normal intake or utilization of vitamins or which cause an increased requirement for them. These include pregnancy, organic gastrointestinal disease, severe or prolonged illnesses of various kinds and dietary restriction for therapeutic purposes. A vitamin deficiency, once acquired, may be prolonged

by resultant anorexia. People with poor appetites tend to select high-carbohydrate foods of low vitamin content.

It is unfortunate that most of the descriptions of pellagra have emphasized the severe forms of the disease. The early symptoms and most of the lesser objective findings were recognized by European investigators and have been repeatedly described. For a thorough review of the literature up to 1919 reference may be made to the monograph of Harris.<sup>2</sup> He<sup>2</sup> and Goldberger,<sup>3</sup> among others, have appreciated that patients without the fully developed picture actually constitute a majority of pellagrins. This is in contradistinction to the old concept that the lesser symptoms occur during an incubation or a prodromal period, more or less prolonged. Harris<sup>2</sup> expresses the opinion that the great majority of pellagrins have suffered for years without ever progressing to the point of the classic condition.

The symptoms of pellagra are extremely varied and often multiple. Not corresponding to any localized organic disease, they commonly simulate some type of psychoneurosis. That the symptoms are functional is literally correct. They are the result of a disturbance in cellular metabolism. Because the correction of this disturbance of function is so easy, the recognition of its nature is of great importance. Removal of patients from the classification of psychoneurosis and the giving of a specific treatment promise to be one of the major accomplishments of medicine.

Although the symptomatology of pellagra is so varied, many of the symptoms are characteristic enough so that, occurring together without demonstrable organic cause, suspicion of their pellagrous etiology should be aroused. There are common signs other than the typical dermatitis which are almost entirely overlooked, and which may be of great value in suggesting the cause

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rather than limited to pressure areas, and in presenting varying degrees of cracking and scaling.

A fairly common type of hyperkeratosis is a more or less diffuse thickening of the skin over the fingers, disproportionate to the use which the hands have had. This is frequently most marked over the knuckles, especially the proximal phalangeal knuckles. The thickened skin may be smooth and white, or it may be fissured and rough and more or less pigmented.

Another common skin manifestation is an ichthyosis-like change, which has received little attention. Harris<sup>8</sup> quotes Calderini<sup>9</sup> and Gemma<sup>10</sup> as describing such a condition, and states that he



FIGURE 2. Finely Roughened Hyperkeratosis over the Elbow

had seen well marked ichthyosis in pellagrins. We have seen a few cases of marked scaling over the greater part of the body which had all the appearance of ichthyosis and which cleared following administration of the vitamin B complex. Much more commonly the changes are less marked, easily overlooked or attributed to chapping. They are not caused by chapping, due to environment alone, because the changes disappear after the administration of the vitamin B complex to ambulatory patients whose environment has not been changed. Nevertheless, environment is undoubtedly a factor. Ichthyosis is characteristically commoner and worse in the winter and ichthyosis-like pellagrous scaling may be conditioned by exposure to cold or heat.

The usual site of ichthyosis-like changes is the anterolateral aspect of the calves (Fig. 4) less frequently the forearms. The edges of the plaques may or may not be loosened. They are usually separated by areas of normal appearing skin. When the deficiency is severe, there may be mottled lines of erythema between the plaques. In a few cases

the plaques are large and thick, simulating alligator skin.

A similar change is the occasional occurrence of an appearance of the skin over the legs which looks, by Stannus's<sup>11</sup> description, as if a smooth layer of lacquer had been applied and then cracked mosaic fashion. Sometimes the skin is uniformly smooth and shiny. Sometimes it may show a mosaic pattern of wrinkles only when it is relaxed ahead of traction in one direction. When severe there may be a yellow brown pigmentation, and the skin over much of the body may resemble that of a well roasted turkey.

A fine, branny desquamation has long been associated with cachectic diseases and with pellagra. It may be the result of poor hygiene, but if it persists or recurs after a few days of hospitalization it is significant. An irregular exfoliation of large, thin flakes may be seen, especially over the trunk.

Lesser changes than a red, sore and atrophic tongue may suggest a pellagrous stomatitis, although they are not always diagnostic. Occasionally the tongue is simply swollen, showing indentations from the teeth. It may appear normal except for redness with swelling of the fungiform papillae about the anterior edges and tip. At times the large, red fungiform papillae are seen against a background devoid of filiform papillae. There may be a heavy coat, usually not extending over the reddened up and sides. This may desquamate overnight, leaving a beefy red tongue. The desquamation may be irregular and progressive, giving the appearance of a "geographic tongue." Fresh deposits may then give areas with varying thickness of coat. Fissuring of the tongue has frequently been said to follow repeated attacks of pellagra. It has been fairly common in our chronic cases, but our observations do not afford proof of its etiology. Aphthous ulcers should all ways suggest the possibility of a pellagrous etiology.

The nervous and mental symptoms, short of dementia or psychosis, are exceedingly varied. Loss of energy, fatigability and weakness are usual complaints and may constitute the presenting symptoms. Other symptoms or signs of deficiency may be absent, or may be recognized only after particular search for them. These symptoms require consideration of hypothyroidism and other conditions such as chronic infection. A number of our patients had previously received thyroid medication with doubtful benefit.

Vertigo is common, as is uncertainty of balance, and sometimes staggering without vertigo. Occasionally tinnitus is described. The head may feel dull, and difficulty in concentration may be

experienced Cephalalgias vary from a sensation of fullness or pressure, localized or general, to boring or stabbing pains

Paresthesias occur, such as numbness, burning or an itching or tingling sensation in the extremities and, less frequently, over the head

A feeling of tenseness, irritability, mental depression and emotional instability are fairly common Patients weep without cause. Insomnia is a frequent complaint It has been known that

differentiation from similar symptoms of intrinsic etiology When there is mucus in the stools, mucous colitis may be simulated Abdominal discomfort may also be simply a feeling of over saturation after a small meal, one of weight in the epigastrium or a distressing sensation of bloating The indigestion accompanying gall-bladder disease may be simulated by such discomfort occurring shortly after or during meals

With a moderate deficiency, anorexia generally

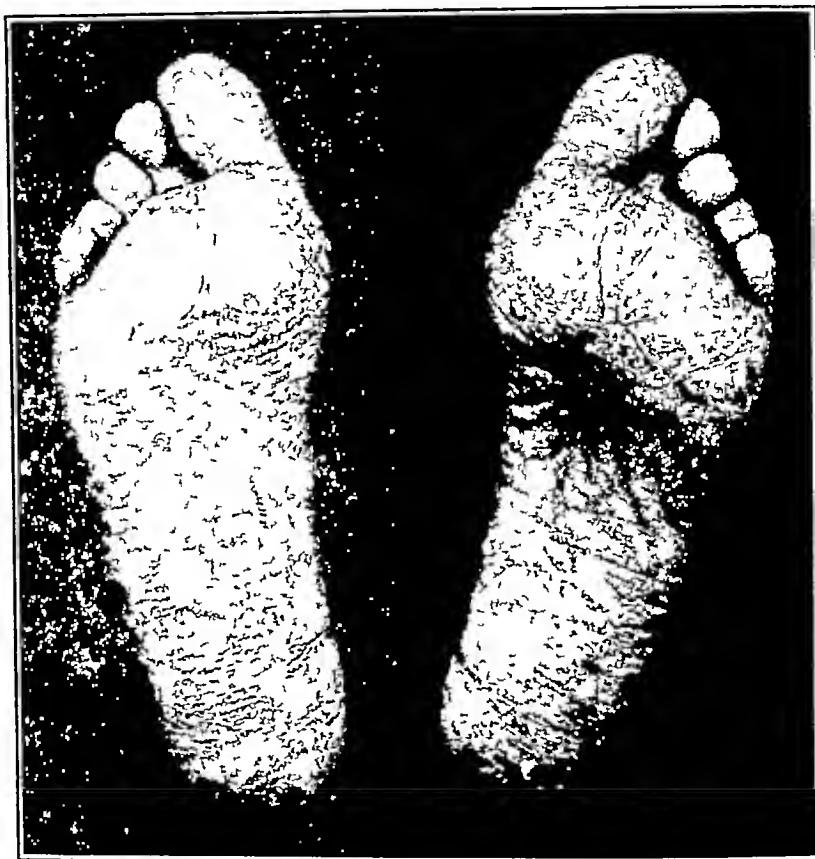


FIGURE 3 *Hyperkeratosis over the Soles*

*The lesions are unlike ordinary calluses they are not limited to pressure points There is characteristic cracking and desquamation*

tremors occur in pellagra We have observed several patients with subjective sensations of internal tremors simulating those of hypoglycemia, except that they occurred without relation to the taking of food They have been associated with minor skin changes and have been relieved after vitamin supplements

Among gastrointestinal symptoms, constipation is perhaps the commonest and earliest With a more severe deficiency, short spells of diarrhea may be interspersed with it. There may be peristaltic unrest and varying pains over the abdomen, which may become a severe colic These symptoms are those of an irritable colon, and require

occurs With a severe deficiency, food may be almost completely refused and vomiting may be serious There may be a salty, bitter or "rotten" taste in the mouth Occasionally there is increased salivation

One of the most distinctive symptoms, usually denoting a fairly severe deficiency, is epigastric burning during or shortly after the ingestion of food, particularly acid food With an esophagus, foods may burn "all the way down" Occasionally the burning is continuous, causing a frequent desire for cold water Otherwise the abdominal symptoms of pellagra may simulate so many other conditions that their evaluation must depend on

association with skin lesions, some of the more distinctive nervous symptoms and a history of an inadequate diet.

From a large number of cases with signs and symptoms of a pellagrous type of deficiency, the following, uncomplicated by organic disease, are presented. They are representative of moderately severe deficiencies with more or less characteristic symptoms. They were all cases of referred



FIGURE 4 *Ichthyosis-like Scaling*

*This cleared after no change in regime other than the administration of vitamin B complex*

patients who had had considerable previous medical attention

Case f F R., a 20-year-old housewife, had not been well since a pregnancy 18 months previously. After delivery she had had a complete paralysis of the legs for 2 weeks, followed by a slow recovery of function. For an unknown reason, the urine and blood pressure were said to have been normal—meat, fish and eggs had been withdrawn from the diet during the last 2 months of pregnancy. The presenting complaints were a feeling of exhaustion, marked, painless weakness of the legs after climbing one flight of stairs, middle-of-the-night insomnia, vertigo, uncertainty of balance so that she had to watch her feet while descending stairs, a burning sensation over the face and a feeling of fullness in the lower abdomen.

On physical examination the patient was obese. The skin over the elbows and knees was mildly thickened and that over the insteps was moderately thickened and pigmented, with a fine serration and branny scaling. The tongue was reddened about its tip. Vibration sense of the ankles was moderately impaired.

The diet as described was not definitely inadequate. The patient was put on a 1500-calory reduction diet and given a supply of tablets of yeast and liver concentrate, supplemented with nicotinic acid. After 1 week she reported marked improvement in symptoms. The skin was not significantly changed. The tongue appeared normal. She still required an afternoon rest.

One month later she felt completely well and was playing tennis for the first time in 2 years. The skin over the elbows and knees appeared normal. There were still slight thickening and pigmentation of the skin over the instep.

CASE 2. V L., a 37-year-old housewife, had for many years had indigestion consisting of distention belching and nausea. During her first pregnancy 7 years before, she vomited almost daily and had one hematemesis. Since then she had had intermittent sharp pains in the epigastrium extending over every part of the abdomen and unrelieved by soda and occasional vomiting. During a second pregnancy 4 years later she had frequent emeses for 5 or 6 months and marked salivation.

On admission the patient was again pregnant, the last menstruation having occurred 2½ months previously. Emeses had become increasingly more frequent for 1 month. She had a burning pain in the epigastrium, to relieve which she drank cold water frequently. Previous constipation had increased and sharp pains over the abdomen were worse. The patient had become nervous and irritable, slept poorly and had occasional vertigo, twitching of the outer eyelids, headaches and a burning sensation over the upper trunk and head. Her weight had dropped from 260 to 230 pounds.

The dietary history was inconsistent. The patient had apparently had a somewhat inadequate high-carbohydrate diet for years which became worse when she was pregnant.

Physical findings aside from an enlarged uterus were obesity, mild hyperkeratosis over the elbows, an ichthyosis-like scaling over the legs and markedly diminished vibration sense in the ankles. Two days after admission the patient developed overnight a brownish-red erythema over the knees (acute pellagrous dermatitis) which cleared in a few days without treatment.

X-ray examinations of the upper gastrointestinal tract, gall bladder and colon were normal. Urinalysis and the Kahn reaction were negative. The total serum protein was 6.6 gm. per 100 cc., with 3.3 gm. of albumin and 3.3 gm. of globulin. The blood ascorbic acid was 0.27 mg per 100 cc. The urinary excretion of vitamin B<sub>1</sub> before and after a test dose was subnormal.

The patient was given 1.5 gm. of nicotinic acid in 5 days, followed by 40 mg. three times a day. At the same time she was given vitamin B<sub>1</sub> 5 mg. four times a day. After 8 days she reported much improvement. She had slept well for 2 nights, had only occasional mild burning sensations over the head or in the epigastrium and had no more sharp pains in the abdomen. She was then given as a source of the whole vitamin B complex liquor hepatis (U.S.P.  $\lambda$ ) 15 cc. four times a day supplemented by nicotinic acid, 20 mg. four times a day.

Two months later having taken the medication irregularly she reported feeling well most of the time, except for being somewhat fatigued. She had had a few spells of

nausea and burning in the epigastrium, which she thought were relieved by taking the medication more regularly. The ichthyosis-like scaling over the legs and hyperkeratosis over the elbows had disappeared except for a few loose flakes over the right elbow.

CASE 3 C M, a 36-year-old housewife, had had a scaly skin since the age of 4, but had felt well until a pregnancy 9 years previously. Following delivery she lost 20 pounds in weight, which she never regained. She became fatigued easily and had an empty feeling in the midabdomen, which was relieved by the taking of food. Five years before she had been very weak and nervous and had had an intermittent diarrhea. Symptoms then abated somewhat but had been much worse for the last 7 months. The patient complained of nervousness, insomnia, choking sensations, frequent numbness of the hands, arms and ears, a "bad sensation" in the head and uncertainty of balance *without true vertigo*. She had a burning sensation in the epigastrium, increased by swallowing tomato or orange juice.

The diet consisted of low-vitamin foods except for one small serving of meat and one serving of carrots, peas or green beans a day.

Physical examination showed a moderate redness and enlargement of papillae over the tip of the tongue. The skin of the entire body was thickened and rough. Over the trunk there were large, thin, desquamating scales. Over the legs there was a marked ichthyosis-like scaling.

The patient was given powdered yeast, 45 gm daily, supplemented with nicotinic acid, 240 mg daily for 6 days, then 120 mg daily.

Two weeks later she reported marked improvement in symptoms. She still became fatigued easily and had early morning insomnia. Three weeks later she was much stronger, slept well and had no abnormal sensations. At this time the skin was normal except for a few thin flakes over the trunk and some thickening of the skin over the legs, which was smooth and shiny, without scales.

In these three cases, symptoms arose during pregnancy. All the patients had chronic skin lesions. In Case 2 they were not marked, but an acute pellagrous erythema over the knees developed during observation. All the patients had characteristic nervous symptoms, including paresthesias, vertigo or uncertainty of balance and insomnia. In Cases 2 and 3 there was epigastric burning, aggravated by acid foods. Weakness and fatigue were pronounced in all the cases.

CASE 4 W K., a 49 year-old man, a seed tester, had for 1½ years had intermittent, severe, colicky pains in the left upper quadrant, radiating to the left back, where there was also a burning sensation. During the physical examination the pains caused him to stiffen and wince. They were relieved following a gurgling in the left side of the abdomen. He had also had considerable constipation, weakness, spells of faintness and vertigo, dyspnea on moderate exertion and a weight loss of 28 pounds.

The diet had not been definitely inadequate before the present illness but had become so because eating induced the pains. The patient took two glassfuls of milk a day, less than one egg a day, meat rarely and green vegetables about once a week.

On physical examination there was moderate tenderness over the palpably spastic colon. There was no abdominal distention or visible peristalsis. The skin over the dorsum of the hands and forearms and over the knees was what thickened, dry and rough, this condition ascribed to his occupation. There was no x-ray evidence of intestinal obstruction.

Treatment was started with nicotinic acid, 60 mg three times a day for 5 days, followed by 60 mg three times a day, and thiamin chloride 5 mg four times a day, followed by 5 mg daily.

At the end of 10 days the patient reported that he had practically no abdominal pain after the 3rd day of medication. He felt stronger, had a good appetite and could eat foods that formerly precipitated pain—tomato juice among others. His only residual symptom was a burning sensation in the left lumbar region, present a slight degree much of the time and aggravated by drinking anything hot or a small amount of alcohol. There was no tenderness in the costovertebral angle. The patient was given a supply of tablets of yeast and liver concentrate. One month later he reported continued improvement. He had regained all his lost weight and normal energy.

In Case 4 the skin changes were not marked and the abdominal symptoms were strongly suggestive of intestinal obstruction, so that the weakness, vertigo and other symptoms were considered secondary until the absence of intestinal obstruction could be demonstrated.

CASE 5 R F, a 41-year-old broker, began 3 months before admission to have a full feeling in the epigastrium immediately after eating and occasional sharp pains in various parts of the abdomen. Constipation of many years' duration had become worse and strong laxatives were being used. He had become nervous and tired and had internal quivering sensations, especially under strain. He had occasional spells of visual disturbance, sometimes blurring, sometimes "dancing vision" and sometimes blanking out of part of the visual field. Two months previously he had had a tight sensation at the heart, relieved by a week's rest in bed. Since then he had been more dyspneic than usual on climbing stairs or flight of stairs.

Physical examination showed no remarkable findings except a branny scaling over the legs. An electrocardiogram was not abnormal.

The patient ate meat once or twice a day, but rarely had milk, eggs or green vegetables.

He was given a supply of tablets of yeast and liver concentrate. Three weeks later he reported marked improvement and had gained 5 pounds. The constipation and abdominal discomfort had been completely relieved. He felt less tense and had had no recent quivering sensations or visual disturbance. The skin of the legs was no longer scaly.

In Case 5 a branny scaling over the legs, the only objective evidence of deficiency, and visual disturbances were unusual. The relief of constipation was noted by the patient without suggestion by the examiner.

Case 6. I. C., a 54 year-old housewife was first seen in 1931 when her chief complaints were weakness and vertigo. She had not been well for many years, having a variety of symptoms including numbness and tingling of the hands and arms. Six years previously she had had a nervous breakdown, with the chief symptom extreme weakness, from which she had only partially recovered. She had had occasional vertigo for many years. Recent spells had been particularly severe, and since the last one there had been a feeling of insecurity of balance without vertigo.

Physical and laboratory findings gave no indication of organic disease. A neurological consultant reported the finding of glove hypalgesia in both arms and made the diagnosis of hysteria.

The patient was seen again 7 years later when her chief complaints were weakness and fatigue. She continued to have mild spells of vertigo. Physical examination again revealed no significant findings except some thickening of the skin below the patellas.

The diet was of doubtful adequacy no milk or eggs, one small serving of meat, one vegetable other than potato and one salad, usually lettuce, each day. Because of this, the nature of the symptoms and the mild skin change, she was given a supply of tablets of yeast and liver concentrate. Two months later she reported complete well-being. Her diet was improved, and 8 months later she reported continued good health.

Case 7. B. M., a 41 year-old single woman school teacher had been below par since having bronchopneumonia 7 years previously. Her mother's health and finances had worried her and for 3 months she had been completely exhausted, nervous and irritable. For a month there had been short spells of vertigo and faintness. Recently there had been some insomnia.

She rarely ate meat or eggs and the chief vitamin-containing foods in the diet were one glassful of milk and one green vegetable a day.

On physical examination the patient presented the appearance of marked fatigue, but there were no abnormal findings other than undernourishment.

She was given a supply of tablets of yeast and liver concentrate. Four months later she felt very well and had gained 12 pounds in weight. She had lost her appearance of fatigue.

The following December she reported having had a very good summer in the country swimming and playing tennis every day. She had had fish daily and abundant vegetables. On returning to work her diet had become more deficient than ever milk being usually omitted. For 6 weeks she had been tired and irritable, and had had occasional vertigo and an occasional drawing sensation in the abdomen. She was given dietary instruction and a supply of yeast and liver-concentrate tablets. Four months later she reported that she had felt very well through the winter.

Case 8. L. A., a 39-year-old, single woman school teacher had been well except for chronic sinusitis and constipation until 1 year before, when she had had a "strep-tococcal sore throat which kept her from work for 5 weeks. Following this attack she had been listless, weak and easily fatigued. Ten weeks previously she began to have burning pains in the epigastrium immediately after the ingestion of food, particularly acid foods, and sharp pains in various parts of the abdomen. For 2 months she had had occasional mild vertigo and three episodes of watery diarrhea lasting half a day each. Three years previously the basal metabolic rate had been reported to be -10 per cent. She had taken thyroid during the winter months

for 2 years and thought that it had somewhat helped her fatigability.

The physical examination and laboratory findings were normal. X-ray examinations of the chest upper gastrointestinal tract, colon and gall bladder were normal. She had a normal gastric acidity.

According to a detailed history both before and after the x-ray examinations, the diet had been quite adequate. In addition the patient had been taking a multiple-vitamin preparation with a low vitamin B<sub>2</sub> assay. Nevertheless, the abdominal pains spells of diarrhea, fatigue and vertigo seemed so suggestive of pellagrous symptoms that she was given a trial of nicotinic acid 60 mg five times a day for 4 days and then 20 mg three times a day.

Three weeks later she reported that on the 4th day of this medication she had noted an abrupt change and was able to eat very well without discomfort. Since then there had been an occasional half hour or hour of dull ache in the left upper abdomen not related to meals, which was steadily decreasing. There had been no recurrence of diarrhea or vertigo. During the next month the abdominal pain completely disappeared and she felt well and strong. The patient then realized that she had not been healthy since her high school days.

Case 9. D. W., a 56-year-old farmer had not been well following a respiratory infection 1 year before. He had had dyspnea on exertion and fatigue so that he was unable to do more than occasional light chores. He had had abdominal distention belching and epigastric burning after eating acid foods. He had had a period of "clumsiness" of the feet. He was irritable, and manifested character changes which made his family fear that he was becoming insane.

The diet included meat, eggs, two glassfuls of milk and fresh vegetables each day.

The chief physical findings were absence of vibratory sense in the legs, and skin changes. The tongue and mouth were normal. There were gross thickening and some fissuring of the skin of the fingers and hands. There were erythema thickening and scaling over the elbows. Similar changes were more marked over the knees (Fig 1) with light pigmentation about the border. There were patches of scaling over the lateral aspect of the lower third of the legs. The skin behind the ankles and over the toes was grossly hyperkeratotic. The soles were moderate ly thickened.

X-ray films of the chest showed a bilateral chronic (fibroid) pneumonitis, which did not change during the period of observation. There was normal gastric acidity.

The patient was given 60 gm. of brewer's yeast daily. Five weeks later he reported general improvement and a gain of 4 pounds. He was stronger but still unable to do much work. He had had but little abdominal distention and no pyrosis. There was a definite but not marked improvement in the skin lesions. He was then given nicotinic acid, 400 mg daily for 1 week and 120 mg daily thereafter with 20 gm. of brewer's yeast daily.

Two months later he reported further symptomatic improvement. He had been doing all his farm work for 3 weeks. The abdominal symptoms had disappeared and the mental outlook was improved. The skin was normal except for some pigmentation over the knees and slight scaling over the lateral aspect of the leg.

Cases 7 and 8 had symptoms without objective evidence of deficiency. In Case 9 the symptoms followed a respiratory infection of which a chronic



fibroid pneumonitis was apparently the residuum. In Case 7 the patient dated her ill-health to an attack of bronchopneumonia seven years previously. In Case 9 the skin lesions with their erythematous bases showed evidence of acute as well as chronic activity—a rare occurrence with us. Cases 8 and 9 gave histories of adequate diets. It will be desirable to confirm by chemical studies that an occasional individual can have a pellagrous vitamin deficiency while taking a normal diet. Neither of these patients had gastric anacidity.

### DISCUSSION

It is apparent that pellagra presents no uniform clinical picture. It may cause important and sometimes serious symptoms without the classic dermatitis and sometimes without the lesser chronic skin lesions. Such cases will be overlooked unless the various symptoms and the lesser objective manifestations of pellagra are kept in mind. The gastrointestinal symptoms, except pyrosis, are seldom distinctive. However, their association with skin changes and with nervous symptoms like paresthesias, vertigo, some cephalalgias, depression and emotional instability may be significant. Occasionally, symptoms may be suggestive enough to warrant a trial of vitamin supplements despite a history of a seemingly adequate diet and the absence of objective signs of deficiency, as in Case 8.

The possibility that a pellagrous type of deficiency may be a common cause of symptoms brings to discussion several considerations. We have become reluctant to accept many diagnoses of psychoneurosis without taking a detailed dietary history and searching for objective signs of deficiency. It is recognized that a psychoneurosis may be a predisposing background for the development of a nutritional deficiency. In such cases, relief of superadded symptoms should be worth while. It need hardly be said that organic disease should be excluded before a diagnosis of deficiency is accepted without reservation. A deficiency state may develop secondary to organic disease. On the other hand, there are many cases in which extensive investigation is not of immediate life-saving importance. In these the psychotherapeutic and reassurance value of such investigations may not warrant their expense before making a test of vitamin therapy.

It may also be said that many patients who present chronic skin and tongue changes admit no symptoms that seem ascribable to a deficiency. (It has been noted above that the significance of hyperkeratoses must be evaluated with due regard to the amount of irritation to which the skin has been submitted, and that ichthyosis-like scaling is

especially common in cold weather.) In such cases the diet should be improved, but vitamin supplements do not seem necessarily indicated unless the patient is about to undergo a serious operation. In that event, they would seem indicated in order to assure an optimum cellular metabolism.

Recent observations have clarified considerably the problem of the treatment of pellagra. Symptoms are contributed by deficiency in various factors of the vitamin B complex, but nicotinic acid has proved to be of outstanding importance. It is present in relatively small amounts in natural materials used as therapeutic sources of the vitamin B complex. A good yeast contains about 0.5 mg. per gram, and a good liver extract for oral use contains about 1.0 mg. per gram. Therefore, for practical therapeutic and economic reasons, synthetic nicotinic acid is recommended as the backbone of the treatment. Curative doses of nicotinic acid ranging from about 100 to 500 mg. or more per day<sup>12, 11</sup> have been reported. The limiting factor in dosage is the flushing reaction caused by nicotinic acid. This reaction is a pharmacologic effect of the acid while it is accumulated in the blood stream awaiting synthesis into its amide and the higher compounds that are the effective vitamins<sup>14</sup>. Such reactions do not occur following the administration of nicotinic acid amide. We have found doses of 60 mg. six times a day satisfactory in producing prompt results without causing uncomfortable reactions in most patients until an adequate total dosage has been approached. When significant reactions occur regularly, the size of the dose, and later its frequency, may be reduced until the patient is taking from 80 to 160 mg. per day in three or four doses. In some patients not under close observation it may be desirable to start treatment with frequent 40-mg. doses.

For the rest of the vitamin B complex, natural sources are recommended, at least for the present. The observations of Sebrell and Butler<sup>15</sup> indicate that a minimal curative dose of riboflavin for cheilosis or angular stomatitis is 0.025 mg. per kilogram of body weight per day. This dosage, then, should give reasonably prompt results in any lesser riboflavin deficiency. Using the smaller reported figures for riboflavin equivalence to a Sherman unit of vitamin B<sub>2</sub>, this dosage may conservatively be considered to be afforded by 600 to 700 such units daily for an average-sized individual. Doses of most natural products with this amount of vitamin B<sub>2</sub> contain amounts of vitamin B<sub>1</sub> which are adequate unless a definite polyneuritis indicates additional supplements. Little is known concerning human requirements for other factors of the complex. That they are of importance is

suggested by some experiences, such as that of a patient with a psychosis, dermatitis and glossitis who became oriented and no longer maniacal after large doses of nicotinic acid, remained stationary for two weeks during the consecutive administration of thiamin and riboflavin, and became normal after taking the whole vitamin B complex.

The above figures represent curative doses for cases with severe deficiencies. Smaller doses may be sufficient for some individuals who are not severely depleted. Inadequate doses, however, will produce disappointing results.

With doses like the above there should be obtained pronounced improvement in gastrointestinal and nervous symptoms in less than a week. For complete relief it will be necessary, in a few cases, to continue for some time the administration of larger amounts of nicotinic acid than the follow-up doses suggested above. Chronic skin lesions sometimes clear completely within two or three weeks, sometimes only after many weeks, and occasionally they show only partial improvement after long continuation of the whole vitamin B complex in larger doses than suggested above.

After the deficiency has been relieved it is desirable to improve the diet so that further vitamin supplements will not be needed. In some pathologic conditions this may not be possible. It seems that occasionally an apparently normal individual needs vitamin supplements in addition to a presumably normal diet.

The question of nomenclature for the types of cases under discussion arises. The terms "pellagra sine pellagra" and "subclinical pellagra" do not seem appropriate for deficiency states that are the cause of clinical disability, although the classic dermatitis is lacking. These terms imply an obscurity that does not stimulate an alertness to

detect the condition. Certainly the cases with chronic skin lesions herein described justify the descriptive name pellagra. It seems justified to extend the use of the name to those cases, lacking any skin lesions, which have the same symptoms and which are relieved by the same vitamin supplements. There are many precedents covering similar situations in medicine. More important than the name, however, is the recognition that such cases do occur, and not infrequently.

#### SUMMARY

Evidence has been presented of the frequent occurrence in the northern part of the United States, among the better as well as among the poorer economic classes, of important disabilities due to a pellagrous type of deficiency. The symptoms are reviewed, and the frequently occurring but commonly overlooked objective manifestations of the condition are described.

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## DIRECT VISUALIZATION OF THE PLACENTA BY SOFT-TISSUE ROENTGENOGRAPHY\*

A LOUIS DIPPEL, M.D.,† AND WEBSTER H BROWN, M.D.‡

BALTIMORE

IT HAS long been a rule that every gravida who has vaginal bleeding during the last trimester of pregnancy should be examined vaginally. Since the main purpose of the examination is to establish or rule out the diagnosis of placenta previa, the procedure entails insertion of the finger through the cervix and palpation of the area immediately surrounding the internal os. The dangers of such an examination are obvious, namely, precipitation of fresh hemorrhage, introduction of infection and initiation of premature labor. Realizing the disadvantages of vaginal examination in these cases, various investigators have attempted to localize the placental site by other methods.

More than a century ago, when Kegardec<sup>1</sup> first described the uterine soufflé, he believed that it was of value in determining the location of the placenta. This sound, of course, is the result of the passage of blood through dilated uterine vessels, and while such vessels are naturally more numerous beneath the placental site, the findings are not dependable. Steele,<sup>2</sup> however, is of the opinion that auscultation of the abdomen after the sixth month of pregnancy will indicate the approximate location of the placenta in at least 75 per cent of cases. Rectal examination has also been employed, but this not only carries with it the danger of precipitating hemorrhage, but is often inconclusive.

Erhardt<sup>3-5</sup> and Katsuya<sup>6</sup> were the first to localize the placenta with the aid of roentgen rays. They injected Thorotrast (thorium dioxide solution) intravenously into experimental animals. This method was suggested to them by slightly earlier work done to visualize the liver and spleen in human subjects and in animals. These organs produce a shadow in the roentgenogram, since the radiopaque thorium is stored in the reticulo-endothelial cells of the liver and spleen and remains in the maternal blood sinuses of the placenta for some hours. Shute and Davis<sup>7</sup> repeated this work with other thorium preparations, and made exhaustive pathological studies of the organs of mothers and their offspring. Thorium has been found to be extremely toxic for many vital organs,

and has a narrow margin of safety. Especially large doses are required for visualization of the liver and spleen, and even with these, immature placentas are often poorly visualized or cast no shadows at all. The maximum intensity of the placental shadow may not appear until hours after the injection of thorium, thus unduly prolonging the diagnosis of placenta previa in cases of vaginal bleeding. There is a tendency toward induction of labor and some reason to suspect permanent sterility as a result. The placenta seems to be an effective barrier to the passage of thorium preparations, for the drug has never been demonstrated in the fetal tissues and the babies appear normal. Thorium itself is radio-active, so that the drug stored in maternal organs for months is quite undesirable. Furthermore, Schmidt<sup>8</sup> warns against the possible danger of further x-ray examination of patients who still have a radio-active drug retained in their tissues. In the light of these studies, it seems difficult to understand how any one could suggest the clinical use of such a dangerous substance.

Amniography, an aid to localization of the human placenta by means of x-ray photography, was introduced in 1932 by Campbell, Miller, Menees and Holly.<sup>9</sup> An aqueous solution of strontium iodide was injected into the amniotic cavity by way of a lumbar-puncture needle inserted through the anterior abdominal and uterine walls. The gestational sac cast a shadow on the x-ray plate and the placenta appeared as a filling defect. Several investigators have employed this method, and various radiopaque dyes have been used: Uroselectan (Kerr and Mackay,<sup>10</sup> Burke<sup>11</sup>), barium sulfate (Burke), Neoskiodan (Cornell and Case<sup>12</sup>), and Perabrodil (Burke). There have been serious objections to the use of this method, and it has not been widely employed. The chief objection is the inherent danger to the abdominal contents of blindly inserting the needle through the abdominal and uterine walls, although there have been no published reports of injury to the intestines. A second objection is the possibility of trauma to the fetus, placenta or umbilical cord. In each case reported by Cornell and Case the placenta was pierced, but in the light of Snow and Powell's<sup>13</sup> observations this is not a surprise, for in each case they chose for the site

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of entrance the side of the maternal abdomen opposite the fetal back. Again, they found that in 2 of their 6 cases the umbilical cord had been punctured. A third objection to this method is the great possibility of induction of labor. Burke found labor setting in so regularly after the injection of Uroselectan that he purposely attempted induction

the sites of injection and appear as streaks on the x-ray plates. In actual practice, however, these results were not observed with any degree of certainty, and the method carries all the inherent dangers enumerated for amniography.

Indirect placentography, accomplished by studying the size and shape of the space between the

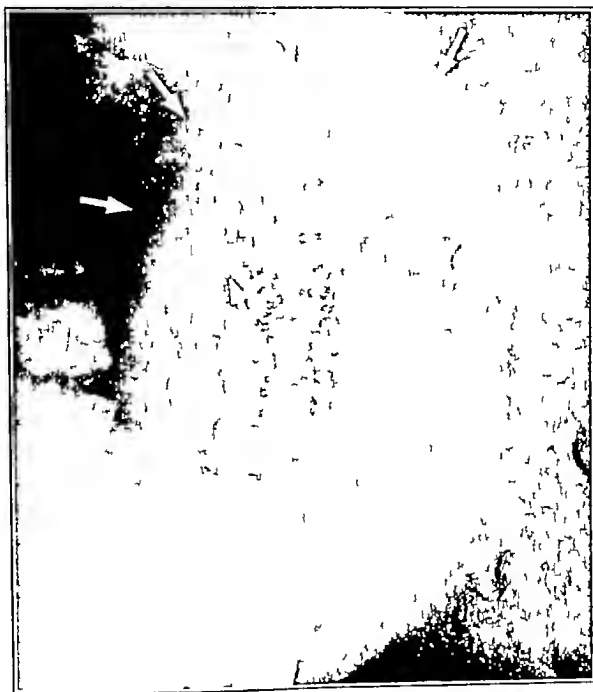


FIGURE 1

*Roentgenogram of a young primipara (E.P.) with a normal pregnancy taken at term. The placenta is implanted over the posterior uterine wall well up in the fundus.*

of labor by this means in 27 cases, failing in only 1, a case of hydramnios.

Hewitt<sup>14</sup> attempted to inject Lipiodol directly into the placenta implanted over the lower uterine segment, by selecting various sites in the wall of the vagina through which to insert the needle. If the placenta was successfully injected with small quantities of the dye, the latter were expected to appear on the roentgenogram as small globules. If the placenta was located in the fundus, the injected Lipiodol was expected to gravitate away from

posterosuperior wall of the urinary bladder, previously injected with a solution of sodium iodide, and the lower margin of the presenting fetal head, was introduced by Ude, Weum, Urner and Robins.<sup>15</sup> Moderately good results have been reported in selected cases by McDowell,<sup>16</sup> Hall, Curran and Lynch,<sup>17</sup> Melver,<sup>18</sup> Friedman and MacDonald,<sup>19</sup> Priest,<sup>20</sup> Jablonski and Meisels,<sup>1</sup> Wells,<sup>2</sup> Beck and Light<sup>3</sup> and Williams.<sup>4</sup> The normal cystocephalic space in late pregnancy measures not more than 1 cm. on the roentgenogram. It appears larger whenever the placenta or any other

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calified patches which might be useful in the diagnosis of placenta previa. Occasionally one sees the placenta in roentgenograms taken for purposes of pelvimetry, but always independent of calcification.

The introduction of soft tissue roentgenography has opened a promising field in all branches of

gynecology. In the majority of cases the placenta was located by observing the site at which the uterine wall appeared to be unusually thickened. On the roentgenograms it measured about 7 cm. at the point of greatest thickness and tapered off toward the periphery. In practically all cases the ventral surface of the fetus faced the placenta,



FIGURE 3

*Roentgenogram from a secundipara (C. G.) with moderately profuse vaginal bleeding beginning ten days before the estimated date of confinement. The roentgenogram shows the placenta implanted over the lower anterior wall of the fundus. Labor was induced and the hemorrhage controlled by a large Voorhes bag. A clinical diagnosis of low implantation of the placenta was made at delivery (Vernon and extraction).*

medicine for by its use one may visualize the soft tissues with the same detail as one does the osseous structures in conventional roentgenograms. The technic employed is essentially the same as that used in ordinary roentgenography. This method has been developed in general medicine, particularly by Carty<sup>27, 28</sup> while Snow and his co-workers<sup>12, 29, 30</sup> have introduced it into obstetrics.

In 1934, Snow and Powell<sup>12</sup> reported a study of 60 pregnant women by means of soft-tissue roent

and in none was the fetal back directed toward it. Very often a knee, an elbow, a foot or a hand of the fetus caused a pressure defect in the placenta. Snow and Powell believed that visualization of the placenta very low in the uterus, or failure to visualize it would aid greatly in establishing the diagnosis of placenta previa. Snow<sup>29</sup> later reported the successful diagnosis of several advanced extrauterine pregnancies. This was made possible by noting the absence of the uterine wall

around the gestational sac. More recently Snow and Rosensohn<sup>30</sup> have pointed out the value of locating the placenta in patients who have previously been delivered by cesarean section. In the event of anterior attachment of the placenta in a subsequent pregnancy they recommend another cesarean section, in order to avoid the added risk of rupture of the uterus. In cases of suspected

definite deterring factors which rendered visualization difficult or impossible. The placenta cannot be visualized in cases of hydramnios, and only occasionally in cases of multiple pregnancy. Unusual obesity of the mother renders visualization more difficult. Prematurity has not offered any great obstacles, and although with immature fetuses the chances of visualization are definitely re-

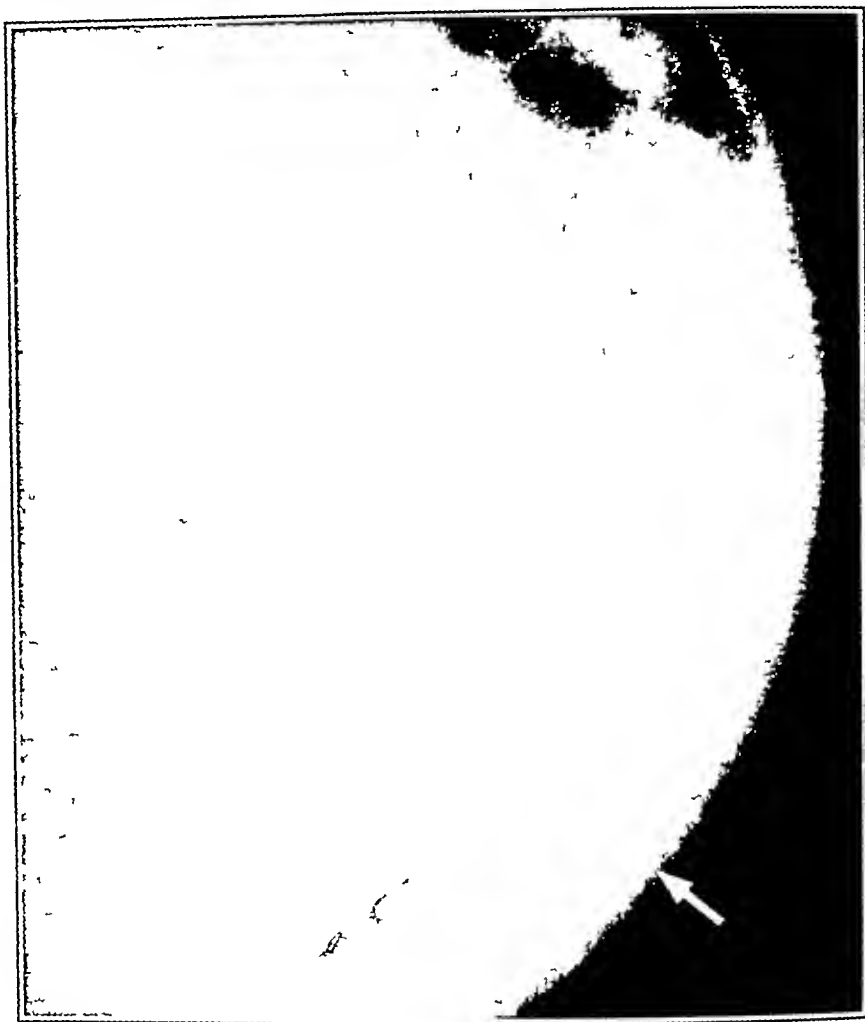


FIGURE 4

*Roentgenogram from a secundipara (I C), taken in the thirty second week of pregnancy on account of painless vaginal bleeding following intercourse. The roentgenogram shows the placenta extending only a short distance up the anterior wall of the lower uterine segment. A diagnosis of central placenta previa was ventured and confirmed by vaginal examination and at cesarean section.*

placenta previa they also employ aerocystograms, in order to study the cystocephalic space.

During the last eighteen months we have employed soft-tissue roentgenography in examining almost 200 pregnant women, roughly one fourth of these patients were x-rayed on account of bleeding in the last trimester. The placenta was clearly visualized in approximately 90 per cent of the cases. In the remainder there were certain

deduced, we have been able to demonstrate the placenta clearly in a pregnancy advanced to only the twenty-fourth week. The position of the fetus in no way deters good visualization. When the placenta is implanted over the lower uterine segment, its lower margin is usually not perceived. However, if one reasons that the normal placenta at or near term covers approximately one fourth of the surface area of the uterine wall, as has

been demonstrated by Torpin,<sup>21</sup> the probable type of placenta previa may be diagnosed with reasonable accuracy. In a small percentage of these patients the location of the placental site was checked at cesarean section or by vaginal examination and in no case was the roentgenological diagnosis found to be erroneous. Moreover, the future course

er have shown that the placenta is usually attached to the relatively flat anterior or posterior uterine wall, and Torpin,<sup>21</sup> with a new method of studying placentation, has recently confirmed this. He found that the placenta seldom extends over the dividing line between the anterior and posterior walls, either laterally or over the apex of



FIGURE 5

*Roentgenogram from a primipara (N P) taken in the thirty-eighth week of pregnancy because of suspected moderate hydramnios. The roentgenogram shows a large fetus in vertex position with a calcified placenta attached to the u hole of the anterior wall of the fundus.*

of the pregnancy in all cases was in conformity with the roentgenological diagnosis. Two illustrative x-ray plates are shown in Figures 1 and 2. Since we adopted this technique the number of vaginal examinations made to determine the cause of bleeding has been greatly reduced. After being x-rayed, many patients are discharged to carry on the pregnancy and to be delivered normally at or near term. A single lateral roentgenogram is usually sufficient. We have not found the anteroposterior view of any particular aid. Earlier writ-

ers have shown that when it does it is apt to be a placenta bipartita, succenturiata or spuria. For this reason the placenta is almost invariably located on a lateral roentgenogram.

While the most important use of soft-tissue roentgenography in obstetrics is in cases of suspected placenta previa there are other applications of the technique which offer possibilities.

We agree with Snow and Rosensohn<sup>20</sup> that the preoperative knowledge of the location of the placenta, regardless of the type of contemplated op-



eration, is of distinct value. Thus, before performing a cesarean section on a patient with an anteriorly located placenta, one might wish to take additional precautionary measures in the way of facilities for transfusion. One might conceivably care to choose between a classical and a low cer-

Before the advent of soft-tissue roentgenography, there was no method of determining the condition of the old cesarean scar in subsequent pregnancies. By means of visualizing the comparative thickness of the anterior uterine wall and the smoothness of its outline, which is made possible



FIGURE 6

*Roentgenogram from a thirty-eight-year old multipara (A A) with an ectopic pregnancy who was admitted two months after her calculated date of confinement and four months after the cessation of fetal movements. She had had slight vaginal bleeding just after fetal death, but none thereafter, and she observed that the abdomen had grown progressively smaller. Soft tissue roentgenograms were obtained, but not interpreted before laparotomy. Note the thin walled gestational sac, the dead fetus and the non pregnant uterus over the lower anterior wall of the product of conception.*

vical cesarean incision, depending on whether the anteriorly implanted placenta were situated in the lower uterine segment or in the fundus. Again, exact knowledge of the site of attachment before the insertion of bougies for induction of labor will guide one in selecting the anterior or posterior wall of the uterine cavity for this purpose, and thus lessen the possibility of separation of the placenta

by the soft-tissue technic, it may be possible to ascertain the soundness of the old scar. To date we have seen 2 cases in which the anterior uterine wall in a pregnancy subsequent to a classical cesarean section appeared to be irregularly thinned, and it was believed unsafe to allow these patients to go through normal labor. This thinning was subsequently confirmed at operation. Further in



SUBDURAL HEMORRHAGE IN PATIENTS WITH MENTAL DISEASE\*

A Statistical Study

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FOR twenty years the Department of Mental Health of the Commonwealth of Massachusetts has maintained a pathologist and a laboratory. The duties of this physician have been to investigate the sudden and unexpected deaths occurring in state mental hospitals, to give assistance to the resident pathologists in the several state hospitals and to perform the duties of resident pathologist in hospitals which lack such officers. From the beginning of the service in July, 1914, to July, 1934, 3100 autopsies were performed, for the most part by the same operator, Dr Myrtelle M Canavan. The protocols of these cases have been investigated in order to determine how often subdural bleeding occurred among patients who died while confined to mental hospitals. The majority of the patients in the series were residents of Massachusetts and although some racial differences occur among them, they were for the most part of similar stock. An additional factor which favored uniformity was the similarity of standards for diagnosis and treatment in the hospitals from which the material was obtained, all of which are under the administration and supervision of the Department of Mental Health.

There is considerable range in the medical vocabulary of terms describing the lesion dealt with in this study. It is therefore advisable to indicate some of the commoner terms that have been used in the past to describe intracranial bleeding of subdural location. Those most commonly encountered are subdural hemorrhage, subdural hematoma, hematoma of the dura mater, hygroma, subdural blood cyst, meningeal blood tumor and pachymeningitis hemorrhagica interna. Additional terms are listed and their sources given by Robertson.<sup>1</sup> For the purpose of this study, the term "subdural hemorrhage" is used according to the definition of Dr Canavan "Extravascular blood in any condition or amount between the dura and arachnoid." Cases in both acute and chronic stages of this condition are included in this se-

ries, ranging in extent from the presence of fluid blood and blood clots, with or without membrane formation, to a thin, brown membrane attached to the under surface of the dura. However, we cannot state definitely the size of the lesions, since only a few of the autopsies were done by one of us (A M A). Two cases were found in which the end result was calcification, and there were a few bilateral hematomas.

Of 3100 autopsy protocols examined, there was evidence in 245 cases (7.9 per cent) of subdural hemorrhage of varying degree and in varying locations. In 117 cases death was due chiefly to disease of the nervous system (Fig 1). In 87 cases

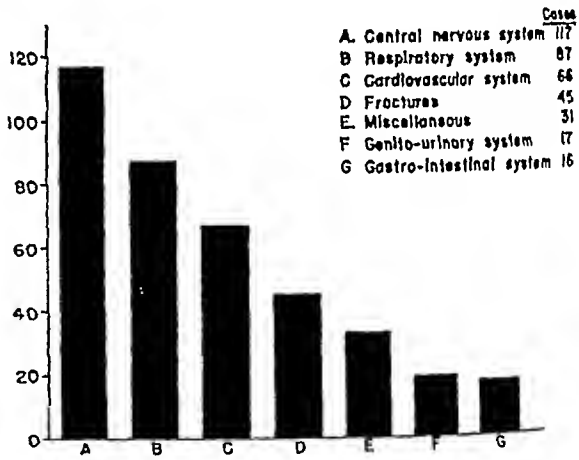


FIGURE 1 Causes of Death Classified According to the Body Systems in 245 Patients with Subdural Hemorrhage

disease of the respiratory system was the primary cause. In 66 cases there was evidence of severe cardiovascular disease, and in 45 death was believed to be caused by complications of fractures, chiefly of the skull. In the few remaining cases death was due to genitourinary and gastrointestinal conditions and a few miscellaneous causes.

In the group of patients who died of neurologic disorders, the conditions most frequently observed were intracranial tumor, meningitis, hydrocephalus, edema of the brain, laceration of the brain, dementia paralytica and tabes dorsalis. In 35 of these cases subdural hemorrhage was the primary cause of death. Forty-five additional cases showed

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other types of intracranial bleeding, that is, extradural, subarachnoid and intracerebral hemorrhages. There were 35 cases of dementia paralytica.

Deaths due to pulmonary disease were next in order of frequency. Bronchopneumonia caused death in 44 cases and lobar pneumonia in 19. Pulmonary tuberculosis was the primary cause in 21 cases. Pulmonary edema, empyema, gangrene and emboli were occasionally reported. Diseases of the heart and the circulatory system were considered to be the chief cause of death in 66 cases.

Trauma was frequent in this series, and fractures were extremely numerous. There were 29 skull fractures and 18 fractures of other bones in the group of patients with subdural hemorrhage; the incidence of fractures was 191 per cent.

Three cases of suicide are included. They were due respectively to a wound in the head, hanging, and slashing of the throat. Relatively few persons died of primary disease of the genitourinary system, in the 17 cases so diagnosed, chronic interstitial nephritis occurred most frequently. Pyelonephritis, cystitis and ruptured bladder were other conditions of importance. The smallest number of deaths were due to gastrointestinal disease.

The weight and height of the patient at the time of death were not always recorded, so that an estimate of the general state of nutrition can not be exact. However, it has been shown<sup>2</sup> that the general body condition and nutrition of patients with mental disease, as evidenced by the weights of specific organs, are somewhat inferior to those of patients who have been in general hospitals for only a short time before death.

All the patients in this series were insane with the exception of 2 who were mentally deficient.

When classified according to psychiatric diagnosis, the highest percentage (150) was found in the group of cases diagnosed as psychosis with other brain or nervous disease.<sup>3</sup> Generally the exact neurological disease was unspecified in the autopsy report. In many cases which show a large subdural hemorrhage at autopsy, the association of a psychosis with vague neurologic signs gives a clinical picture suggestive of syphilitic or alcoholic origin or of brain tumor. It was exceptional to find subdural hemorrhage listed as an etiologic factor in patients receiving the above psychiatric diagnosis.

A survey of the literature indicates the general agreement among the students of this condition that subdural bleeding is a commoner postmortem finding among psychotic patients than it is among general hospital patients. Wiglesworth<sup>4</sup> found 54

cases (84 per cent) in 637 autopsies and Lewis<sup>5</sup> found 81 cases (79 per cent) in 1565 autopsies. In our series, there were 345 cases (79 per cent) in 3100 autopsies. At the Boston City Hospital, a general hospital, Munro<sup>6</sup> observed 215 subdural hemorrhages among 1203 cases of head injury selected for neurosurgical treatment. These patients were admitted over a six year period and all had suffered trauma. There are few data available that give the incidence of subdural hemorrhage among general hospital patients, and available autopsy data in general hospitals do not report the incidence, since in most general hospitals a postmortem examination of the skull contents is not regularly made unless the clinical examination suggests some lesion in the brain. In view of this fact, reliable statements in regard to the incidence of subdural hemorrhage in nonpsychotic patients are rare. In our 3100 autopsies, it is important to note that in almost every case the skull was opened and the contents examined.

In considering why subdural hemorrhages are found more commonly at autopsy among psychotic patients than among general medical patients, Robertson<sup>1</sup> stated in 1900 "They occur most commonly in the insane of a somewhat advanced age, and are found in the great majority of instances in patients in whom the mental disease has been of long standing. The form of insanity that furnishes the largest proportion of cases is general paralysis." Althaus<sup>7</sup> expressed similar views in 1878 when, speaking of the occurrence of subdural hemorrhages among mentally sound patients, he stated that they occurred "in the *old decrepit worn-out intemperate*," and were not infrequently associated with low forms of pleuropneumonia, pneumothorax, pleurisy, pericarditis, emphysema, rheumatic fever, delirium tremens, leukaemia, pernicious anaemia, scurvy, haemophilia and the various forms of Bright's disease of the kidneys." He added "It has occasionally been developed in the course of whooping cough from excessive venous congestion brought on by severe paroxysms of coughing, and injury to the head may also lead to it. Subdural hemorrhage has been reported to occur in association with typhus fever, chronic alcoholism, infantile scurvy and tuberculosis.

Our incidence of subdural hemorrhage of 7.9 per cent may appear excessive, but several factors warrant consideration. Many patients had psychoses definitely associated with organic intracranial disease, such as cerebral arteriosclerosis and dementia paralytica. Trauma may have been commoner in this group of patients than among nonpsychotic persons.

<sup>3</sup>Organic but not specifically classified (Table 2)

Among the 245 patients with subdural hemorrhage, 148 (60.4 per cent) were men and 97 (39.6 per cent) women, a ratio of 1.5:1 (Table 1)

TABLE 1 *Distribution of Cases of Subdural Hematoma According to Age and Sex*

YEARS	MALES	FEMALES	TOTAL
0-10	1	0	1
11-20	3	0	3
21-30	5	2	7
31-40	14	10	24
41-50	27	18	45
51-60	33	11	44
61-70	30	29	59
71-80	18	19	37
81-90	17	6	23
91-100	0	2	2
Totals	148	97	245

Brain<sup>7</sup> claims a greater preponderance of men over women, in the proportion of approximately 5:1. The findings of Leary<sup>8</sup>—chiefly medicolegal—more nearly approximate the proportion found in our series, he reports 50 cases of subdural bleeding in which there were 34 men and 16 women, a ratio of approximately 2:1.

In our series cases of subdural hemorrhage were found among patients who died in all decades of life (Table 1, Fig. 2). The greatest number (59)

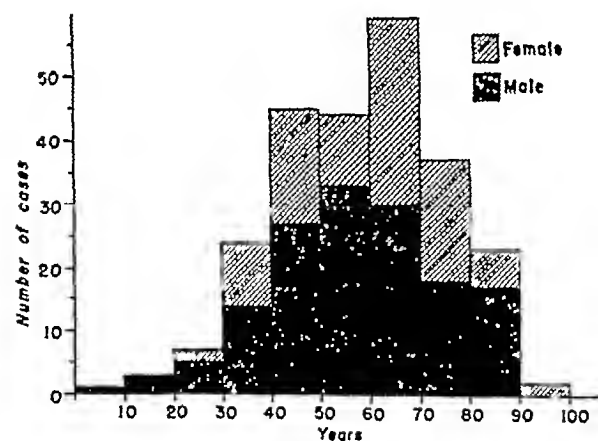


FIGURE 2 *Sex Distribution and Age at Death in 245 Patients with Subdural Hemorrhage*

were found in patients who died between sixty and seventy years of age. One case was that of a boy who died before his tenth year. Two women died between ninety and one hundred. There were almost twice as many patients between forty and fifty at death as there were between thirty and forty.

The largest number of male patients were between fifty and sixty years old at death. There was a steady increase by decades until the sixty-year mark was reached, after that there were fewer cases. There were no female patients with subdural bleeding who died between one and twenty

years of age. There was an irregular distribution by decades after that age until the seventh was reached. In this decade the largest number of cases occurred. There was a rapid decrease in number of cases in the eighth, ninth and tenth decades. An interesting frequency of occurrence was noted in the fifth decade (18 cases), whereas there were relatively few cases in the fourth (10) and the sixth (11).

The range of ages at death appeared to be approximately the same for both sexes. The personality of male patients in respect to aggressiveness and activity may be considered as a factor in producing subdural hemorrhage. Among women, a more protected situation and lesser activity may tend to limit its incidence. The factors of alcoholism, syphilis and trauma may contribute to the difference in sex incidence among male patients, and these factors may be more important than among women. Subdural hemorrhage among women may occur as a result of changes more dependent on cerebral vascular conditions than is the case among men.

When classified according to psychosis, 79 patients were found to have had mental disorders associated with old age, such as cerebral arteriosclerosis and senile conditions (Table 2). The

TABLE 2 *Psychiatric Diagnoses in All Autopsied Cases and in Those with Subdural Hemorrhage*

PSYCHIATRIC DIAGNOSIS	NO OF CASES AUTOPSED	CASES WITH SUBDURAL HEMORRHAGE	
		NO.	PER 1000 CASES
Psychosis with other brain and nervous diseases	101	16	159
Epileptic psychosis	178	22	124
Dementia paralytica	338	35	104
Psychosis with cerebral arteriosclerosis	417	43	103
Senile psychosis	413	36	87
Alcoholic psychosis	192	16	83
Dementia praecox	576	35	61
Psychosis with mental deficiency	234	11	47
Manic-depressive psychosis	171	8	47
Undiagnosed psychosis	116	3	26
Psychosis with somatic disease	158	3	19

frequent finding of subdural hemorrhage among these patients may be related to the presence of other findings such as marked brain atrophy, with a consequent increased size of the subdural and subarachnoid spaces. The brain atrophy that occurs in elderly patients may cause a strain on unsheathed pial veins after the brain and dura separate. The emaciation, malnutrition, weakness and unsteady gait of elderly persons may render them more liable to trauma.\* Further research is indicated in order to place these poten

\*Vitamin C levels in the blood plasma have been shown to be significantly low in a group of patients suffering from senile psychoses and psychoses associated with cerebral arteriosclerosis.

nal factors in a true causal-consequential sequence.

Next in size after the group of patients with senile psychoses are those with dementia praecox and dementia paralytica (35 each). The pathological findings in these psychoses when uncomplicated are so dissimilar that an explanation of the occurrence of subdural bleeding is difficult.

Although the number of patients with dementia praecox in mental hospitals is greater than that of patients with dementia paralytica, and although more of the former come to autopsy, the fact that 35 cases in each group showed subdural bleeding indicates a much greater frequency in patients with dementia praecox. This does not seem consistent with the fact that organic changes which favor subdural bleeding, such as vascular disease, brain atrophy and hydrocephalus, are frequently present in cases of general paresis. Both psychoses may be regarded as equally liable to physical trauma.

Epileptic patients with subdural hemorrhage (22 cases in 178 autopsies) form the next group in order of size. Among these the finding of subdural hemorrhage is readily explained by the frequency of seizures and the associated head trauma, resulting in skull fractures and in some cases brain damage.

Among the 22 epileptic patients, 11 died with fractured skulls. It was believed that the subdural hemorrhage was directly due to recent head injuries and skull fractures, although it is conceivable that the bleeding found at the autopsy was due to previous head injury. There were 2 other epileptic patients with recently fractured ribs, a total of 13 cases with known major trauma out of 22 epileptic patients in whom hemorrhage was found. The factor of trauma seems more important than the possibility of brain changes with advancing age. Exactly half the epileptic patients were under fifty years of age.

For purposes of classification, 4 cases of tabes dorsalis were included among the "psychoses with other brain and nervous disease," since there was some doubt whether syphilis was the sole etiologic factor in these patients.

There were 16 cases with alcoholic psychoses. The factor of alcoholism is only remotely related to the subdural hemorrhage, since most of the alcoholic patients were over fifty years of age and had been hospital residents for a long time. None were under thirty years of age. There were 2 between thirty and forty, 3 between forty and fifty, 5 between fifty and sixty and 6 between sixty and seventy. The mean age was fifty-four.

The use of alcohol was not the exclusive factor in producing psychoses among these patients. Per-

sonality defects were common, and unspecified neurologic disease may have been masked by the symptoms of alcoholism in many cases. Head injury following drunkenness is a remote possibility because of the long hospital residence. In a few of these cases there had been known trauma of various kinds. Trauma as a direct and exclusive factor was found to account for only 3 cases.\* Organic brain disease and birth trauma may help to produce the condition.

Eleven cases of subdural hemorrhage were found in patients diagnosed as having psychosis with mental deficiency. They were distributed in the various age decades as follows: 2 each in the second, fourth and fifth, 4 in the sixth and 1 in the seventh.

In the affective disorders subdural hemorrhage was a comparatively rare finding. There were 8 cases with manic-depressive psychoses and 5 with involutional melancholia.

The studies of subdural hemorrhage cited above are in general agreement as regards the importance of senility, syphilis, alcohol and trauma in producing the condition. In our study the cases cited may be rearranged to corroborate the earlier findings in part. There were 79 cases with psychoses associated with old age, that is, psychoses accompanying cerebral arteriosclerosis and those due to senile changes. Thirty-eight patients had been committed because of syphilis of the central nervous system (dementia paralytica and psychoses with cerebral syphilis). Sixteen cases with alcoholic psychoses and 3 with traumatic psychoses have been discussed. The factor of senility can be considerably emphasized if the elderly cases with dementia praecox and other psychoses are considered. In these, the patients had lived for years in a mental hospital before death.

Other psychiatric diagnoses were represented by a few cases. The seven minor diagnostic groups totaled only 18 cases.

The factor of nutrition and vitamin reserve is probably a significant one. It is at present receiving great attention and will doubtless tend to modify the prevailing concept that trauma is the most serious etiologic factor in this condition when the incidence of subdural hematoma in a group of patients with infrequent history of trauma is compared with the incidence in

\*Obviously this figure is not representative, for the diagnosis was not made during life or even suspected by the clinical condition of these patients. The diagnosis of subdural hemorrhage in almost every case was made at postmortem examination. Head injury was the obvious factor in producing 3 of the 3 cases of traumatic psychoses, but trauma as an etiologic factor may have been overlooked in a large number of elderly infirm patients, steadily gaining who had suffered fall and fractures, those with hyperactive behavior irritability, and dementia or disposition and those with special accidents resulting in head injury. Thus, trauma appears more important in producing subdural bleeding among psychotic patients than in producing psychotic behavior.

a large series of cases with known severe head injuries. In the series of cases with severe head injuries reported by Munro the incidence was 18 per cent, while in our series it was 79 per cent.

It was possible to ascertain in 209 cases whether the lesion was unilateral or bilateral and, if unilateral, whether the lesion was on the right or left side (Table 3). Most hemorrhages were found

TABLE 3 Location of Subdural Hemorrhage

LOCATION	NO. OF CASES
Unilateral or bilateral	
Unilateral	122
Right	64
Left	58
Bilateral	87
Unstated	36
On convex surface or base	
Solely convex surface	207
Solely base	20
Convex surface and base	18
Brain area*	
Frontal area	27
Parietal area	23
Temporal area	13
Occipital area	12
Cerebellar area	1

\*Fifty cases are represented in this subgroup. In several more than one area was involved.

over the convex surface of the brain and relatively few were exclusively over the base. In many cases, the subdural bleeding, although its presence was noted, was not fully described with respect to location. However, the descriptions were sufficiently accurate in 50 cases to state exactly which regions of the brain were mainly affected. In some cases more than one region of the brain was involved,—for example, the frontoparietal or the temporoparietal areas,—but the lesions in the frontal or parietal areas predominated. They were involved twice as frequently as the temporal and occipital regions. In at least half the cases the lesion was unilateral, as previously noted by Leary,<sup>8</sup> and this finding is important from an etiologic standpoint. Diseases of the blood vessels, the chief cause of brain atrophy (if accepted in any case as the sole cause of bleeding), is usually bilateral in distribution and should accordingly cause bilateral hemorrhage. The cases of subdural hemorrhage in patients with dementia paralytica were more frequently bilateral than was the case in other groups.

Extreme variations were noted in the size of the lesions. A few were described as small, circumscribed hemorrhages amounting to little more than "subdural flecking." In these, definite areas of bleeding could be seen under the dura, small in size and without evidence of the effects of pressure on the underlying brain tissue. They were probably fresh lesions in many cases, and possibly terminal in origin. This appearance was

very pronounced in patients dying of respiratory disease, for example, pulmonary tuberculosis. A few lesions of this type were noted in epileptic patients who died of asphyxia.

The majority of hemorrhages were large and diffuse and usually involved considerable subdural space and extensive areas of the brain. It was common to find lesions extending over an entire lobe or pressing on the major part of the surface of two or more lobes, or even on the entire hemisphere. Lesions were frequently found which pressed on two hemispheres, or occasionally one hemisphere and the corresponding basal surface of the brain. The lesions varied in consistence from that of fresh blood to that of calcification, with the intermediate state predominating in which membranes surrounded the clotted blood, suggesting the formation of subdural cysts.

A rough determination of the age of the lesion was made from the condition of the blood. Liquid blood or a soft clot without a membrane was accepted as evidence of a recent lesion. Membrane formation with orange-brown pigmentation of the inner dural surface was taken as evidence that the hemorrhage was old. Every stage between these points was found, but the latter was commoner. It is noteworthy that atrophy was occasionally more marked beneath these rusty areas. Two extreme cases were found in which a layer of definite calcification had formed beneath the dura. Both occurred in mentally defective patients, and the lesions may have been the result of injury at birth. These cases showed positive evidence of recent subdural bleeding, and blood in all states, as well as membranes in several areas, was present. Multiple membranes were described occasionally in cases of dementia paralytica with subdural hemorrhage.

The age distribution demonstrates the increase in subdural hemorrhage with advancing years, but also shows that the condition is not unknown in earlier years. The psychiatric diagnosis in this series shows the relation of organic brain changes to subdural bleeding. Subdural hemorrhages in the insane appear to be a relatively unimportant cause of death. When venous congestion occurred before death, the subdural blood consisted of small, discrete and apparently recent hemorrhages, which were considered to be terminal phenomena. They were found mainly in epileptic patients, in those with dementia paralytica dying during convulsive seizures and in some with pulmonary tuberculosis and pneumonia.

There seems to be little connection between the age of the lesion and the duration of the psychosis except in a few acute cases with a fatal termina-

tion soon after admission. In a few cases, mental deficiency may have been caused by subdural hemorrhage together with birth trauma, but it is possible that there was other cortical damage.

In certain cases, rusty pigmentation and membrane formation on the inner side of the dura suggest that the lesions were at least one year or more in age. In some cases there was a blood clot of recent origin as well as one surrounded by a membrane, showing that a recurrence of bleeding is possible. This was best illustrated in cases of dementia paralytica and mental deficiency.

#### SUMMARY AND CONCLUSIONS

Two hundred and forty five cases of subdural hematoma were found among 3100 consecutive autopsies of psychotic patients, an incidence of 7.9 per cent.

Presumable etiologic factors, such as trauma, avitaminosis, senility, alcoholism and syphilis, are discussed.

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### CLINICAL AND POTENTIAL ALLERGY IN FAMILIES WITH ALLERGIC CHILDREN\*

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THE incidence of clinical allergy in the general population has been variously estimated between 7 and 10 per cent. Such estimates have been based on surveys compiled by Cooke and Vander Veer,<sup>1</sup> Piness and Miller,<sup>2</sup> Vaughan,<sup>3</sup> Rowe,<sup>4</sup> and others. Similarly, the incidence of clinical allergy in the families of hypersensitive patients has been placed between 40 and 60 per cent. These calculations have been based on case histories alone. Sometimes such histories are taken casually with little attention paid to some of the less spectacular symptoms, which, nonetheless, often suggest allergy.

The incidence is of interest partly because the inheritance of allergy merits a more careful study and partly because the early recognition of allergy in the family can frequently lead to a prevention of symptoms. It was decided, therefore to apply the same method of investigation to the entire family as is applied to the individual allergic child. To this end, when a child with definite allergy applied for treatment all other members of the immediate family available at that time were subjected to the same allergic survey as was the patient.

The survey consisted first of all in questioning about manifestations of past and present allergy, noting especially hay fever, vasomotor rhinitis, asthma, eczema, urticaria and angioneurotic edema. Skin tests were made on each patient and relative alike, as well as on a few normal control subjects. Estimates of blood eosinophils were not made.

There were 40 allergic patients, their relatives comprised 135 individuals. At the same time, four normal or control families with a total membership of 17 persons were investigated. All ages were included in the relatives and controls.

The relatives of the 40 patients comprised 32 fathers, 40 mothers, 30 brothers and 33 sisters. Of these, 40 (30 per cent) presented evidence of either present or past allergy as determined from their histories. None of the 17 members of control families, on the other hand, gave evidence in their histories of any of the common manifestations of allergy.

Skin tests were made by the scratch (dermal) method, and 35 different substances to which subjects are commonly sensitive were applied. In all, 6912 scratch tests were done, 6300 among allergic children and their families and 612 among the four control families. The same technique and the same substances were applied to the 40 patients,

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the 135 relatives and the 17 control subjects, a total of 192 persons. The results are presented in Table 1, in which the various antigens have been listed according to the frequency with which they caused positive skin reactions. The table does not include those antigens which were positive in less than 6 cases. Cocoa, vanilla, chicken feathers, cottonseed, kapok, beef, lobster and carrots caused reactions in 5, or 25 per cent, of the 192 subjects. Birch, rye, corn, barley and fish did so in only 4 (20 per cent) and beef in 3 (15 per cent),

Peshkin and Rost,<sup>5</sup> who found 0.76 per cent positive and doubtful reactions in 9406 skin tests on normal children.

These figures show clearly that the skin test is still an index of the patient's allergic disposition, and that the more active the allergy, the greater is the incidence of positive reactions. More striking, however, is the fact that the normal subjects among allergic families react more frequently than do those of control families, over 2 per cent against less than 1 per cent.

TABLE 1 *The Incidence of Positive Scratch Tests in 40 Allergic Children, in 135 Relatives and in 17 Non Allergic Adult Controls*

ALLERGEN	40 ALLERGIC PATIENTS	135 RELATIVES				17 NORMAL CONTROLS		TOTAL
		FATHERS 10A 22N	MOTHERS 13A 27N	BROTHERS 8A 22N	SISTERS 9A 24N			
House dust	21	3	4	4	6	3	3	48
Ragweed	17	4	1	3	3	4	2	43
Timothy	11		1	1		1	2	18
Cat dander	8		1	1		2		16
Orchis root	5	1		1	5	1	1	14
Potato	9	1		2	1			13
Horse dander	5		1	1	3	1		12
Rabbit hair	2		1	3	3		3	12
Apple	5	2	1	1	1		2	12
Oats	7	1						9
Banana	5		1	1		1		9
Oak	3	1		2			1	8
Dog dander	2	1		3	1		1	9
Egg	5			1		1		7
Orange	4			3				7
Pear	4			2	1			7
Beans	2		3	2				7
Walnuts	4	1		1				6
Wheat	4	1	1					6
Tomato	3		1	2				6
16 other allergens	33	3	2	13	5	2	5	65
Total positive tests	159	19	18	47	33	9	20	334
Total tests made	1440	360	792	468	972	288	792	6012
Percentage of positive tests	11.0	5.3	2.3	10.0	3.4	3.1	2.5	4.8

while milk and chicken gave positive results in only 1 case (0.5 per cent).

Table 1 shows that in the 40 children with frank allergy, 11 per cent of all the skin tests were positive. The relatives have been divided into two groups: those who gave a history of some manifestation of allergy in the past or present and so were considered allergic (A), and those who failed to give such a history and so were classed as normal (N). Thus, 10 of the 32 fathers were allergic by history, and 5 per cent of the 360 tests made on them were positive. On the other hand, the 22 non-allergic fathers showed an incidence of 2 per cent of positive tests. Likewise, the allergic mothers had three times as many positive tests as did the non-allergic mothers, 10 per cent and 3 per cent respectively, and the allergic brothers and sisters had a correspondingly higher ratio of skin tests than did their non-allergic mates.

In contrast to these results, the total incidence of positive skin reactions in the 17 members of the four control families was less than 1 per cent. These results are in fair agreement with those of

The discrepancy between positive skin tests and symptoms is always important, and as a matter of incidental interest we attempted to correlate the clinical findings with the skin reactions in all patients tested. The data thus gathered are presented in Table 2. It shows, as expected, that

TABLE 2 *Correlation between the Allergic History and the Skin Tests in 175 Members of Forty Allergic Families*

SUBJECTS TESTED	ALLERGIC HISTORY		NON ALLERGIC HISTORY	
	SKIN TEST POSITIVE	SKIN TEST NEGATIVE	SKIN TEST POSITIVE	SKIN TEST NEGATIVE
Allergic children (40)	31	9	0	0
Fathers (32)	7	3	6	16
Mothers (40)	8	5	10	17
Brothers (30)	5	3	8	14
Sisters (33)	5	4	6	18
Totals	56	24	30	65

wherever a history of frank allergy was present the skin tests were usually positive. The reverse is true where a history of allergy was lacking. The figures here also emphasize the relatively high in

idence among the allergic families of individuals who have positive skin tests in the absence of clinical hypersensitivity. That such reactions may be of potential significance has been emphasized by Peshkin and Rost.<sup>6</sup>

Another observation made in the course of this study concerns the frequency with which more than one member of an allergic family may be affected. Thus, eleven families each had 1 member with allergy, twenty-one families had 2 members each, five had 3 each, and three had 4 each.

### DISCUSSION

Certain facts brought out in this study are of direct interest, others of inferential importance.

Of direct interest are the observations that potential allergy is common in each family that has one member with frank allergy. This is evident from the histories of the individual cases and from the number of positive skin tests among the normal members of such families. These potential allergic persons are a challenge to the clinician. If allergy is ever to be successfully treated, it must be recognized before the disease has progressed to an advanced stage. The elimination of wheat, milk or feathers in a patient with corresponding positive skin tests who has only minor symptoms, such as nasal stuffiness or a hacking cough, may ward off a much more serious illness, such as asthma or chronic sinusitis. Kern<sup>6</sup> has recently stressed this point. Particularly in children are preclinical allergic symptoms of allergy common. These early nasal and bronchial symptoms pass off as "colds," "bad tonsils" or "enlarged adenoids," only to assume a form of frank allergy at an older age.

The frequency with which more than one person in a single family may be allergic bears on

the need of a comprehensive survey of all members of such families.

The patient's history is the best guide to the diagnosis of allergy. Exhaustive questioning of the members of our group, with particular attention to the occurrence of symptoms in relation to season, occupation, foods, drugs, environment and so forth, has enabled us to discover definite allergy in subjects who would otherwise have been classified as normal.

The skin tests, whose importance as a diagnostic aid has often been questioned, appear to be a definite and assertive index of allergy.

### SUMMARY

The incidence of clinical allergy is much higher in families with allergic children (46 per cent) than is that among the general population (7 to 10 per cent).

There is a greater incidence of potential allergy among members of allergic families than among members of normal families.

The frequency with which several individuals in single families are allergic bears on the need of comprehensive allergic surveys in these families.

The early recognition of subclinical allergy in allergic families and the elimination of possible sensitizing agents offer an approach to prophylaxis in allergy.

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## REPORT ON MEDICAL PROGRESS

### TRANSFUSION THERAPY\*

A Review of Blood Groups, Transfusion Accidents, Hemolytic Reactions, Stored Blood, Transfusion Methods, and Plasma and Serum Transfusions

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THE major advances in transfusion therapy in recent years have concerned the immunological aspects of blood groups, clarification of the mechanism of certain transfusion accidents, the increased use of stored blood (preserved blood, bank blood), the introduction of methods for preservation by drying of plasma and serums‡, and the use of dilute and concentrated plasma or serum for transfusion. World War I gave great impetus to the transfusion of whole blood containing citrate as an anticoagulant and introduced the use of stored blood on a moderate scale. In World War II it is apparent that stored whole blood, plasma and serum will be tried on a large scale. During the last year two valuable books on blood groups and blood transfusion have been published. The second edition of Wiener's<sup>1</sup> book is an important source for information on transfusion, the technic of blood typing and especially the immunology, heredity and anthropology of blood groups. Riddell's<sup>2</sup> new volume is a most practical treatise on transfusion therapy based on his wide experience. These two books complement each other remarkably well.

The frequency of blood transfusions is a matter of common knowledge.<sup>3</sup> The indications for transfusion of whole blood and of plasma or serum are undergoing change, and depend on what elements of the blood are specifically required by the patient. The major uses for the transfusion of whole blood have been, and still remain, the replacement of hemoglobin for its oxygen-carrying power, and the combating of shock due to loss of blood volume. In bleeding disorders, such as hemophilia, thrombocytopenic purpura and the hypoprothrombinemia of vitamin K deficiency, transfusions of whole blood may be lifesaving.

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†This report is part of an investigation concerning the destruction of red blood cells aided by a grant from the Transfusion Betterment Association of New York City.

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§Plasma is the fluid portion of unclotted blood usually separated from the cellular elements after the addition of an anticoagulant. Serum is the fluid portion which is separated from clotted blood.

Many transfusions are given for supportive treatment, and some for the immune properties of the plasma.<sup>4</sup> It remains to be seen how widely plasma or serum will be employed for the treatment of shock and for the replacement of proteins, prothrombin, clot-promoting substances in hemophilia,<sup>5</sup> immune bodies and readily available food stuffs. It is noteworthy that dogs on a protein free diet can be maintained in nitrogen equilibrium by the parenteral administration of dog plasma.<sup>6</sup> Bock<sup>7</sup> and Riddell<sup>8</sup> have discussed the possible contraindications to transfusion in such conditions as cardiac failure, nephritis, protein sensitivity, hemolytic anemia, leukemia and lymphoma.

The major source of blood for transfusion therapy in the United States is the professional donor.<sup>9</sup> The cost<sup>3, 9</sup> of 500 cc of blood varies from \$25 to \$50. For indigent patients this cost to the family or institution may become economically prohibitive. One large municipal hospital paid \$14,825 in 1939 to professional donors for urgent transfusions. In contrast with the professional system, the British Red Cross Society in 1921 established the voluntary system, in which the donor receives no payment except for traveling expenses, usually amounting to an equivalent of 25 cents. The London service alone had 2378 volunteer donors registered and supplied 6628 transfusions in 1937. Riddell<sup>10</sup> devotes two chapters to a thorough description of the merits and organization of this remarkable service. He emphasizes the low cost—about \$2.25 per transfusion—for administration costs, the high type of donor obtained, the freedom of donors from syphilis, and the method of supervision of the donor's health, which limits the number of times blood may be given to four a year for men and three for women. This volunteer system has proved practical and economical to administer, and permits the unlimited use of transfusions for indigent patients without undue burden to patient or hospital. The administrative costs are defrayed by income derived mainly from fees from private cases, with a smaller contribution by public institutions.

## BLOOD GROUPS

It is of interest to review the recent advances in the immunological aspects of blood groups because of the practical application of these facts in transfusion therapy

*Classifications of Blood Groups*

The extensive use of both the Jansky and the Moss classifications of blood groups has caused confusion<sup>3, 11</sup> because of their conflicting numbers for Groups O and AB of the international nomenclature. As shown in Table 1, the international

is the specific reaction between the agglutino-gen of the red blood cell and the corresponding iso-agglutinin of the serum. Thus A agglutino-gen is agglutinated by  $\alpha$  isoagglutinin but not by  $\beta$  isoagglutinin, and similarly B agglutino-gen is agglutinated by  $\beta$  isoagglutinin but not by  $\alpha$  isoagglutinin. As shown in Table 1, corresponding agglutinogens and isoagglutinins do not exist in the same blood, on the contrary, those isoagglutinins are present in the serum for which there is no corresponding agglutino-gen in the red cells. Accordingly, the blood group of an unknown

TABLE 1 *Classifications of Blood Groups and Subgroups of Human Blood Showing the Agglutinogens of the Red Blood Cells and the Isoagglutinins of the Plasma and Serum*

CLASSIFICATION OF BLOOD GROUPS				AGGLUTINATING REACTS RED BLOOD CELLS	ISOAAGGLUTININ UNUSUAL PRESENT IN PLASMA AND SERUM		FREQUENCY OF GROUPS SUBGROUPS IN 904 INDIVIDUALS UNDER 57 YEARS
MOSS NUMBERING	JANSKY NUMBERING	INTERNATIONAL NOMENCLATURE Group Subgroup			$\alpha$	$\beta$	
IV	I	O			$\alpha$	$\alpha$ $\beta$	44.5
II	II	A	$A_1$ $A_2$	Strong Jodan	$\beta$ $\beta$	$\alpha_1$ (rare) $\alpha_2$	25.6 12.0
III	III	B		Strong	$\alpha$	$\alpha_1$	13.6
I	IV	AB	$A_B$ $A_B$	Weak or nonreactive		$\alpha_1$ (rare) $\alpha_2$	3.1 1.2

Groups and subgroups named for agglutinogens of red blood cell group O red blood cells do not contain A or B agglutinogens one with Group O blood is the so-called "universal donor" and one with Group AB the "universal recipient"

$\alpha$  isoagglutinin agglutinates all red blood cells containing A agglutinogen (Subgroups  $A_1$ ,  $A_2$ ,  $A_3$ ,  $A_4$  and  $A_5$ )

$\beta$  isoagglutinin agglutinates only red blood cells containing B agglutinogen (Subgroups  $B_1$  and  $B_2$ )

$\alpha_1$  isoagglutinin agglutinates all red blood cells containing A agglutinogen (Group B and Subgroups  $A_1$ ,  $A_2$  and  $A_3$ )

$\alpha_2$  isoagglutinin agglutinates red blood cells containing A agglutinogen (Subgroups  $A_4$  and  $A_5$  (weak)) and also those of Group O blood

nomenclature classifies the blood groups according to the presence or absence from human red blood cells of the two agglutinogens,\* A and B, which are the dominant hereditary factors discovered by Landsteiner<sup>11, 1</sup>. The international nomenclature was accepted by the Public Health Committee of the League of Nations in 1929 and is used extensively in scientific publications. It has definite advantages, compared to the numbering systems, since it is free from ambiguity and is based directly on the physiology and genetics of the blood groups. Undoubtedly the international nomenclature should be taught in medical schools and introduced into hospital usage to replace the less definitive classifications of Moss and Jansky.

*Determination of Blood Groups*

Samples of human blood are subdivided into four different groups by observing the presence or absence of agglutination in a mixture of human red cells and serum. When agglutination results, it

blood sample may be determined in two ways<sup>1</sup> by identifying the agglutino-gen content of the red cells, employing test serums of known blood groups, by identifying the isoagglutinin content of the serum, employing test red cells of known blood groups. Since test serums may be conveniently stored they are used routinely for the determination of blood groups, but the use of test red cells is a valuable adjunct to the use of serums.

In the usual technique, three reagents are necessary—a suspension of the red cells to be examined and the two test serums, which are derived respectively from blood of Groups A and B. The blood group is determined by observing the presence or absence of agglutination between the unknown cells and the two test serums. The serum from Group A contains  $\beta$  isoagglutinin that from Group B contains  $\alpha$  isoagglutinin. Accordingly, red cells of Group O are not agglutinated by either serum since these cells contain neither

\*This term refers to the origin of the agglutino-gen in the human species as opposed to heteroagglutinins from another animal species.

\*The specific agglutinable property of the erythrocyte

A or B agglutinin. The cells of Group AB, however, are agglutinated by both test serums since both agglutinogens are present. The cells of Group B are agglutinated by only one test serum, that is, Group A serum containing  $\beta$  isoagglutinin, cells of Group A, on the contrary, are agglutinated only by the test serum from Group B containing the  $\alpha$  isoagglutinin. A variety of technics have been found satisfactory, such as the hanging drop<sup>11</sup> and slide methods,<sup>12</sup> the test-tube procedure of Landsteiner,<sup>11</sup> and the macroscopic technic of Riddell<sup>13</sup> employing undiluted whole blood. The most important safeguard in blood grouping is the use of test serums containing high concentrations of isoagglutinins.<sup>12-14-16</sup> Riddell<sup>10</sup> advises using only those test serums which produce agglutination at a dilution of 1:100. Satisfactory test serums may be purchased from the Transfusion Betterment Association of New York City and from certain pharmaceutical companies. The concentration of isoagglutinins in any serum can be determined readily by testing serial dilutions of the serum with known red cells, as described by Wiener<sup>12-17</sup> and by Riddell.<sup>18</sup>

It has been shown that blood of Groups A and AB can be subdivided, by qualitative differences in A agglutinin, into Subgroups A<sub>1</sub>, A<sub>2</sub>, A<sub>1</sub>B and A<sub>2</sub>B.<sup>19</sup> For a review of this subject Wiener<sup>20</sup> should be consulted. The approximate frequency of occurrence of the subgroups in the United States, as reported by Wiener and Rothberg,<sup>21</sup> is shown in Table 1. There are important practical aspects of the subgroups which concern the routine grouping of blood. The relative average sensitivity, in the agglutination reaction, of the agglutinogens of the subgroups can be represented as follows: A<sub>1</sub> > A<sub>1</sub>B > A<sub>2</sub> > A<sub>2</sub>B.<sup>22</sup> Furthermore, the  $\alpha$  isoagglutinin agglutinates all cells containing A agglutinin, whereas the  $\alpha_1$  isoagglutinin agglutinates only the A<sub>1</sub> agglutinin. The concentration of  $\alpha$  and  $\alpha_1$  isoagglutinins varies widely in serums from bloods of Groups O and B. Such serums containing low concentrations of these isoagglutinins when combined with the weakly sensitive cells of Subgroup A<sub>2</sub> or A<sub>2</sub>B, may fail to produce agglutination in both the indirect grouping test and in the direct crossmatching.<sup>20-23</sup> Under these circumstances, Subgroup A<sub>2</sub> blood can be incorrectly grouped and crossmatched as Group O (no agglutination observed) and Subgroup A<sub>2</sub>B incorrectly designated as Group B (agglutination only by  $\beta$  isoagglutinin).<sup>15</sup> Weak test serum is the direct cause, therefore, of such errors in grouping and is probably responsible for a significant portion of those Group A bloods which are incorrectly grouped as Group O. For a description of

methods for identifying the subgroups, see Wiener<sup>20</sup> and Davidsohn.<sup>23</sup>

### *Isohemolysins*

Isohemolysins are a normal component of human serum and are demonstrable in about 30 per cent of serums containing isoagglutinins.<sup>11</sup> These isohemolysins are group specific, producing hemolysis of the same cells which are agglutinated. Although the isohemolysin cannot be separated from the isoagglutinin, the hemolytic reaction requires the presence of serum complement, whereas the agglutination reaction does not. Since iso-hemolysins frequently are not demonstrable, it is possible to have isoagglutination without isohemolysis, but isohemolysis is always associated with isoagglutination. The largest dilution of a serum that still shows isohemolysis is usually much lower than that dilution still showing isoagglutination. Practically, isohemolysis may occur and may interfere with the agglutination in the direct compatibility test when fresh serums containing complement are used.<sup>11</sup>

### *Problems in Blood Grouping*

From the practical point of view, if the two test serums contain a high concentration respectively of  $\alpha$  and  $\beta$  isoagglutinins, there is rarely any difficulty in classifying red cells correctly into one of the four blood groups (O, A, B and AB). The most dangerous error in blood grouping results from a failure to obtain agglutination, resulting usually from weak test serums.<sup>24-25</sup> A striking case, reported by DeGowin,<sup>24</sup> is that of a donor, incorrectly grouped, who served as a Group O donor in ten transfusions. After three years, when potent testing serum was used, he was found to belong to Group A. The discovery was not made, however, until two patients of Group O had died from hemolytic reactions. Since the crossmatching of donor's and recipient's bloods appeared compatible in these fatal accidents, this emphasizes the limitations of the compatibility test and the danger of incompatible blood mixtures which do not show agglutination in vitro at room temperature.

In the direct compatibility or crossmatching test, which should be performed before each transfusion, apparent incompatibilities are occasionally observed, as evidenced by agglutination.<sup>24</sup> In certain cases, agglutination is expected from a knowledge of the blood groups. For example the serum from Group O should agglutinate the red cells of the other three blood groups. In other cases, agglutination may occur that is not expected from the blood groups involved. In this event it is advisable to carry out the following procedure:

dures recheck the blood grouping, examine the agglutinating potency of the testing serums with known cells, and determine whether the unknown serum agglutinates the red cells from that same individual (autoagglutination). Rouleau formation or pseudoagglutination if observed with undiluted serum is usually eliminated by diluting the serum with an equal volume of physiological saline. So-called "autoagglutinins" may produce agglutination at room temperature of all red cells, including those of the same individual. This reaction is increased at ice-box temperatures and is completely reversible at body temperatures. The presence of rouleau formation of autoagglutinins in the recipient's serum is not a contraindication to transfusion. Incompatibilities have been observed<sup>20-22</sup> between the subgroups of Groups A and AB due to the agglutination of the red cells of one subgroup by the isoagglutinins occasionally present in the serum of the other subgroup as shown in Table 1. A chapter of Wiener's<sup>21</sup> book is entitled "Sources of Error in Blood Grouping."

### Blood Types\*

Landsteiner and Levine have described other agglutinogens of human red cells, designated as M, N and P, which are demonstrated by agglutination reactions with immune rabbit serums. These agglutinogens appear to have no immediate clinical importance in transfusion therapy *per se*<sup>24</sup> but have a well-established significance in the hereditary and medicolegal aspects of blood groups.<sup>21</sup> For a review of these blood types, see Wiener.<sup>22</sup> As stated by Wiener and Peters,<sup>25</sup> "With the agglutinogens A<sub>1</sub>, A<sub>2</sub>, B, M, N, P and Rh, alone, as many as seventy-two different types of human blood are readily distinguished. This fact is staggering, but for the clinical use of transfusion therapy it is essential to consider primarily the blood groups of the international nomenclature, and possibly in addition Type Rh which is discussed below."

### TRANSFUSION ACCIDENTS

The mortality rate from transfusion accidents estimated from large series varies from 0 to 0.5 per cent.<sup>2, 21, 26</sup> Many such deaths are preventable. The reported frequency of nonfatal reactions, including febrile responses to transfusion is significantly higher, varying from 1 to 40 per cent.<sup>2, 21, 22</sup>

Fatal transfusion accidents involving the recipient may be roughly classified as follows:<sup>2, 22</sup> hemolytic reaction, with death from shock or later from

uremia, congestive heart failure or vascular accidents, such as embolism and intracranial hemorrhage, allergic response, with bronchial spasm;<sup>2, 22</sup> hyperpyrexia<sup>2</sup> occasionally reaching temperatures of 112 and 115°F; operative accidents, such as air embolism or intracranial hematoma following transfusion through the fontanel.<sup>2</sup> Nonfatal reactions include the above accidents in milder form, the transfer of diseases such as syphilis, malaria and influenza,<sup>2, 22</sup> and the operative complication of phlebitis. The blood donor occasionally suffers the complication of anemia, syncope or phlebitis, but only with great rarity has death been reported.<sup>2</sup> The prevention of accidents is certainly a most important aspect of transfusion therapy.

Fatal and nonfatal transfusion accidents are in large part preventable provided their causes are understood and avoided. The problems of hemolytic reactions and the compatibility of bloods are discussed subsequently in some detail. The incidence of chills and fever following transfusion can be reduced from 12 to 1 per cent<sup>26</sup> by the elimination of foreign proteins including clotted blood from the transfusion equipment and of pyrogenic organisms<sup>24</sup> from the distilled water that may be used. The proper preparation of solutions, instruments and equipment has been well described by Lewisohn and Rosenthal.<sup>20</sup> Congestive heart failure is usually a contraindication for blood transfusion. In patients without manifest heart disease, however, fatal shock or congestive failure has occurred following severe rigor or an apparently uncomplicated transfusion. Altschule and Gilligan<sup>26</sup> have recently shown that in normal subjects the infusion of solutions of salt or dextrose at the rate of 20 cc. per minute produces an increase in blood volume but only minimal changes in the cardiovascular functions. At more rapid rates they observed an increase in blood volume, together with considerable increases in venous pressure and cardiac output and changes in the electrocardiogram. Many serious reactions would be prevented by the slow administration of blood with an intravenous drip technique and at a drip rate of 40 to 60 drops per minute.<sup>2</sup> The danger of allergic response in asthmatic or hypersensitive patients may be decreased by the biological test described below, and by insisting that the donor be in a fasting state before giving blood. The transfer of syphilis, malaria, influenza and other diseases is controllable by proper selection of the donor. Also, it is frequently possible to anticipate that a patient may require a transfusion. The completion of the arrangements in advance will remove much of the emergency status, which is

\*The bloods contain lag agglutinogens identified by heterologous (animal) serum are assigned to certain types (M, N, P and Rh).<sup>21</sup> In order to distinguish them from the blood groups (O, A, B and AB) which are identified by homologous (human) isoagglutinins.

conducive to making errors. Operative accidents can be reduced to a minimum by employing well-designed simple equipment<sup>31</sup> and by avoiding cutting down on veins, a procedure which is rarely necessary.

### HEMOLYTIC REACTIONS

The rapid intravascular hemolysis in the recipient of the donor's or recipient's red blood cells, with liberation of massive amounts of free hemoglobin, constitutes the most frequently dangerous complication of transfused blood. The pathogenesis of shock following a hemolytic reaction and treatment by an immediate second transfusion of compatible blood are described by Hesse and his co-workers<sup>30</sup>. The reports of Bordley<sup>37</sup> and of DeGowin and his collaborators<sup>38, 39</sup> on the kidney lesion produced by hemoglobinuria deserve detailed study.

### *Mechanism of Increased Blood Destruction*

There is general agreement that increased blood destruction may result from the admixture of red blood cells with plasma containing incompatible agglutinins, hemolysins or both.

It has been clearly demonstrated that hemolysins occurring without agglutinins may produce extreme intravascular hemolysis<sup>40, 41</sup>. Conversely, Ham and Castle<sup>42, 43</sup> have recently shown that the injection into animals of an agent producing extreme agglutination of erythrocytes, but without hemolytic activity in vitro, causes hemolytic anemia, hemoglobinemia, spheroidal erythrocytes and increased susceptibility of the red blood cells to hemolysis in hypotonic solutions of sodium chloride (fragility test). They also demonstrated that sterile incubation of mammalian blood in vitro and intravascular stasis in vivo produce similar changes in the erythrocytes. Consequently, they believe that hemolytic transfusion reactions caused by agglutinins (without hemolysins) may result from the intravascular stasis of agglutinated red cells in the spleen and other organs. As in the test tube, hemolysis results from progressive swelling of the red blood cells to the point of rupture, apparently due to an increase in the osmotically active constituents of the erythrocytes<sup>42, 43</sup>. Similar observations on the effect of stasis on the fragility of erythrocytes have been recently reported by Tsai, Lee and Wu<sup>44</sup>.

In this connection, Wiener and Schriefer<sup>45</sup> have shown that the erythrocytes of blood stored for twenty-one days were destroyed by the recipient in twenty-four hours, with resulting hemoglobinemia and hemoglobinuria. Red cells stored for

so long a period are known to show swelling and a marked increase in hypotonic fragility<sup>46-48</sup>. Presumably they are destroyed in vivo by the above mechanism of further swelling and rupture, which is quite comparable to the destruction of red cells of increased fragility in hemolytic jaundice<sup>42, 43</sup>.

### *Blood Compatibility*

Most hemolytic reactions result from the transfusion of incompatible blood, some result from stored blood that is too old<sup>31, 46</sup>. Fatal hemolytic reactions have resulted when blood of known incompatibility was given, but also when no incompatibility could be demonstrated in vitro. There are, therefore, at least two major problems: the avoidance of incompatible blood transfusions, and greater care in detecting incompatibilities.

The only bloods that are potentially compatible are those belonging to the same blood group and, probably, to the same subgroup<sup>23, 26</sup>. Even here homologous group incompatibilities are demonstrable, as shown below.

The use of Group O blood, from the so-called "universal donor," to transfuse individuals of the other three blood groups introduces plasma from the donor containing both  $\alpha$  and  $\beta$  isoagglutinins, which are not compatible with the red cells of the recipient. Usually, however, these agglutinins are of relatively low concentration and are adsorbed by the red cells and diluted by the plasma of the recipient without harmful reaction. Although large numbers of such transfusions without fatalities are reported, there is a difference of opinion concerning the safety of this practice, as discussed by Riddell<sup>49</sup>. It is apparent that a number of fatal and nonfatal hemolytic reactions have resulted from the use of Group O blood containing large concentrations of  $\alpha$  or  $\beta$  isoagglutinins or both<sup>3, 24, 29, 50, 51</sup>. Coca<sup>52</sup> found that these potentially dangerous universal donors comprised 3 per cent of 350 prospective Group O donors. Therefore, if universal donors must be available for emergency transfusions in other blood groups, it is probably essential to avoid those with a high concentration of isoagglutinins. The concentration of isoagglutinins can be determined readily by serial dilution of the serum, as described by Wiener<sup>17</sup> and by Riddell<sup>18</sup>.

*Homologous Group Incompatibility* Fatal hemolytic reactions have occurred with disturbing frequency following the transfusion of blood apparently of the same group as the recipient's, or following multiple homologous group transfusions from the same donor<sup>24, 26, 53, 54</sup>. In many such cases competent observers have failed to detect in vitro any evidence of incompatibility. One promising advance toward understanding this type

of reaction is the recent description by Wiener and Peters<sup>24</sup> of Rh agglutinin and Rh isoagglutinin in human blood. The Rh agglutinin is independent of the A, B, M, N and P agglutinogens, and is detected by agglutination with serum prepared by immunizing rabbits with the red blood cells of a monkey (*Macaca rhesus*).<sup>25</sup> Human bloods containing red blood cells agglutinated by the heteroagglutinin of this immune serum, and therefore showing the presence of Rh agglutinin, are designated as Type Rh+. Of approximately 100 blood samples tested, those found to be Type Rh+ constituted about 85 per cent, and those found to be Type Rh- only 15 per cent. Accordingly, it is possible to have bloods of any one of the international blood groups which are either Type Rh+ or Rh-. Most donors' bloods are Type Rh+ and transfusion of this blood into an Rh- recipient of the same international blood group with a Type Rh- blood has produced an immune response, that is, the appearance of the Rh isoagglutinin in the blood of the recipient. Subsequent transfusion of Type Rh+ blood into the same recipient has produced reactions, presumably because of the destruction of the Rh+ red cells by the newly formed Rh isoagglutinin. Wiener and Peters emphasize that the agglutination reaction *in vitro* between Rh agglutinin and Rh isoagglutinin is not strong and may occur only at cold temperatures. Two severe hemolytic reactions, one of them fatal, have been observed however, following such homologous group transfusions, coincident with the appearance of Rh isoagglutinin in the serum of recipients with Type Rh- blood who received more than one transfusion of Type Rh+ blood. Wiener and Peters suggest the following technic in addition to the usual grouping and crossmatching procedures as a presumptive test for the presence of incompatibilities due to Rh factors:

Two drops of patient's serum, preferably separated from the clot at refrigerator temperature, are mixed with one drop of the donor's cell suspension in a small test tube (Tube 1).

In another tube a similar mixture of the patient's serum and the patient's cells is set up (Tube 2).

The tubes are placed in ice water for five minutes then centrifuged while still cold and the mixtures gently shaken. The agglutination reaction is observed macroscopically and microscopically. If neither tube shows agglutination the donor is compatible. If both show agglutination an autoagglutinin is present and the donor probably can be used without danger. If Tube 1 shows agglutination and Tube 2 does not, the donor is incompatible.

This evidence serves to re-emphasize the importance of crossmatching blood samples before

any and every transfusion. It is possible that the above compatibility test may detect certain dangerous homologous group incompatibilities.

The subgroups of Groups A and AB have not yet been shown to produce hemolytic reactions<sup>6</sup> when transfusions have occurred within the group, that is, Group A<sub>1</sub> blood given to a Group A<sub>2</sub> recipient. If such reaction occurred as pointed out by Wiener and Peters, it would be necessary also to rule out other sources of incompatibility, such as the Rh factor. However, it is advisable to avoid the transfusion of bloods that can be shown to be incompatible in the crossmatching. Thus far Types M and N have not been shown to be related to hemolytic reactions.<sup>26</sup>

### The Biological Test

The biological test has been emphasized as a valuable adjunct to the prevention of dangerous hemolytic reactions.<sup>6</sup> This test consists of the slow injection, that is, by intravenous drip, of 10 cc. or more of blood, with the observation of any symptoms occurring after twenty minutes of injection such as chill pain or restlessness. If the transfusion is stopped because of a severe reaction, it is unlikely that the injection of as much as 100 cc. of incompatible blood could produce a fatal hemolytic reaction.<sup>26</sup> Furthermore, the urine may be alkalinized in advance of transfusion by administering sodium bicarbonate by mouth.<sup>27, 28</sup> This simple prophylactic procedure may well prevent the kidney complications of hemoglobinuria.

### METHODS OF TRANSFUSION

Concerning the debated question of the direct vs. compared with the indirect methods of transfusion, Riddell's<sup>29</sup> statement is probably an adequate summary. There is, he says, "no reasonable or convincing evidence that therapeutic priority can be awarded to or claimed by either whole or citrated blood, and it is the clinical experience of those who have used and studied both varieties that no difference exists in the results obtained." Both Riddell<sup>29</sup> and Wiener<sup>1</sup> give full descriptions of direct and indirect methods of transfusion.

### STORED BLOOD

The use of stored blood for transfusion, begun in World War I<sup>30</sup> has increased materially. Thus, Wiener<sup>31</sup> collected reports in 1939 of at least 14,000 transfusions of stored blood given in the United States. The technic of setting up a blood bank and collecting and storing blood has been fully described elsewhere.<sup>32, 33-35</sup> Exclusive of war work, the blood bank has been especially useful in large



charity hospitals, where blood from volunteer donors may be collected and used within a few days, and where expert supervision is available. Unquestionably, the proper use of stored blood is an important adjunct to transfusion therapy and, because of the presence of volunteer donors, offers economic assistance to the hard-pressed charity hospital.

The limitations<sup>31-40</sup> of using stored blood vary in proportion to its state of preservation\*. It has been demonstrated that the following changes occur, varying considerably with the type of medium mixed with the blood: the erythrocytes gradually swell, increase in fragility and eventually hemolyze<sup>40-48</sup>, the platelets and white blood cells decrease within twenty-four hours<sup>47-48</sup>, the bactericidal and phagocytic activities are slowly reduced<sup>46</sup>, the prothrombin concentration gradually diminishes<sup>66-68</sup>, certain chemical changes are progressive<sup>70-73</sup>. The maximum period of storage of blood is debated in the literature and variously stated as from two days to two weeks, with most observers suggesting that the blood be used within a week. Red blood cells which are increased in fragility probably are destroyed, after transfusion, at a rate roughly proportional to their fragility. The reactions to transfusions of stored blood have been studied<sup>31-45-74</sup> but require more investigation.

### PLASMA AND SERUM TRANSFUSIONS

Preliminary studies on animals and man are available concerning the transfusion of serum and of plasma, containing sodium citrate as anticoagulant, in the treatment of shock,<sup>75-78</sup> hemorrhage,<sup>76</sup> burns,<sup>79</sup> increased intracranial pressure<sup>80</sup> and hypoproteinemia,<sup>81</sup> and in the prophylactic treatment of infectious diseases.<sup>82-83</sup> In most observations the plasma or serum was preserved by drying, employing one of several methods now available.<sup>84-87</sup> Such dried material is apparently preserved indefinitely, it may be redissolved readily and given in concentrated or diluted form. The use of preserved plasma will probably become an important part of transfusion therapy because of the availability of plasma from stored whole blood, the excellence of preservation, the ease of transportation and the convenience of administration. Theoretically, the indiscriminate transfusion of plasma or serum in large amounts without consideration for blood groups may produce dangerous reactions. The isoagglutinin concentrations may be reduced materially by pooling serums<sup>68</sup> or by mixing citrated blood samples, for example Groups A and B, such that the isoagglutinins and isohemolysins are absorbed by the red cells and thereby removed.<sup>87</sup>

Plasmas or serums known to have low concentrations of isoagglutinins and isohemolysins could be administered, in all probability, without regard to blood groups.

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changing to the right during the convulsions. There was no apparent response to treatment. Stupor increased rapidly. The pulse became weak and rapid, cyanosis appeared, and death occurred on the third hospital day.

### DIFFERENTIAL DIAGNOSIS

**DR. HAROLD G. TOBEY** It is evident that we are dealing with an acute frontal sinusitis which was probably engrafted on a chronic process. We have a history of previous attacks of frontal sinusitis, as evidenced by headaches and occasionally some swelling of the left eye. Let us stop for a moment to consider the possible complications of an acute frontal sinusitis. Infection can extend in two ways. The first is by spread via thrombosed vessels through the posterior wall of the frontal sinus to the dura, and through the dura to the subdural space. The other way is by direct extension through the posterior wall, with necrosis of the bone. There is one significant entry here, that is the extraction of the abscessed tooth. It is true that in the presence of sinus infection, both of the antrum and of the frontal sinus, the extraction of abscessed teeth may light up a previous infection which has been giving very few symptoms. There have been a number of these cases at the Eye and Ear Infirmary, the mode of extension probably being through the blood stream. We have had a number of cases in which, following extraction of teeth, there has been spreading osteomyelitis. However, this patient seemed to be well following the extraction up to fourteen days before admission, when he began to have further symptoms of infection of the frontal sinus, which became progressively worse. Then two days before entry he had a mild chill associated with nausea and vertigo. Knowing he had an acute frontal sinus the chill might possibly have been the beginning of a brain abscess. An acute brain abscess often is associated with chilly symptoms, nausea and vertigo. On the other hand, this may have meant a beginning blood stream infection. The chill was accompanied by pain in the midline of the forehead and vertex. The situation of the pain is in the region of the frontal sinus, but with pain located in this area and with the chill, nausea and vertigo we also have to suspect the beginning of a phlebitis and thrombosis of the longitudinal sinus. The morning before entry there was another severe chill and shortly thereafter the patient developed aphasia and impairment of vision. With the mention of aphasia of course, we immediately begin to think of the Rolandic area and the possibility of some septic focus there. It might possibly have represented the start of a

brain abscess, of a localized meningitis over this area or possibly of an extradural abscess.

There were slight ptosis and edema of the left upper eyelid, with acute tenderness of the frontal sinus. This makes us think of perforation, either through the floor of the frontal sinus or from the ethmoid, and a beginning orbital abscess, but it was accompanied by a stiff neck, which of course immediately brings up the question of meningitis. We will come to that later in considering the spinal fluid.

Next we have the neurological examination and the matter of the eyes. He moved them to the left normally but they did not go beyond the midline to the right. That perhaps is not an unusual finding. I know of no lesion except a central one that would cause that, and I think it is perhaps unimportant. The one important thing about the eyes was the absence of nystagmus. In these acute infections we have to think of metastatic abscesses and the possibility of cerebellar abscess, but the absence of nystagmus at this stage argues against a cerebellar lesion.

The next point of importance is the paralysis of the right arm and leg which of course brings us back again to the left Rolandic area. The superficial reflexes were present but the knee jerks, Babinski and ankle clonus were absent, all of which argue for absence of any generalized meningeal infection. On the other hand we have the history of the stiff neck which is one of the earliest signs of general meningeal infection.

The next important points are the results of the lumbar puncture. The fluid was yellowish, with normal dynamics, a cell count of 427 per cubic millimeter with 400 polymorphonuclears, and a questionable increase in the total protein and the sugar levels. Two days later another lumbar puncture was done, and again the fluid showed an increased protein and an increased sugar. These findings argue against any general meningeal infection. The initial pressure is not mentioned. I imagine it was increased. The 427 cells with the 400 polymorphonuclears are consistent with a local meningitis. The increased protein of course argues for cerebritis with destruction of some brain tissue, but again the practically normal or slightly elevated sugar is against any bacterial invasion of the entire meningeal fluid.

**DR. CHARLES KUBIK** The initial pressure was 310 mm. of water.

**DR. TOBEY** We know that with bacterial infection of the cerebrospinal fluid the sugar is practically always decreased, and this is also consistent with a localized and perhaps somewhat walled-off meningeal infection. We have no report of the

## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 26351

#### PRESENTATION OF CASE

A thirty-seven-year-old caretaker was admitted to the hospital complaining of headache of about five days' duration.

The patient was aphasic on arrival at the hospital, and the history was obtained from his wife. He had always enjoyed good health until the winter before admission, when he suffered with frequent, severe head colds, often associated with swelling over the left eye, and accompanied by the drainage of a profuse, thick, yellow nasal discharge. About six weeks before entry an abscessed tooth was extracted by his dentist. He was well thereafter until fourteen days before admission, when he developed another typical head cold. This persisted, but he continued to work, and four days before admission, while attending the cinema, the left eye began to "water." He developed a progressively increasing pain in it, and in the left supraorbital region, which radiated upward over the forehead. Three days before entry the pain was so severe that he remained home from work. There was no known fever. A local physician was called, who prescribed nose drops for sinusitis. He was recalled a few hours later to administer morphine for the pain which had become excruciating. Two days before admission the patient developed a fever of 102°F, and in the evening had a mild chill, with nausea and vertigo. The pain was located mostly in the midline of the forehead and vertex. On the morning before entry the patient, obviously worse, had a severe shaking chill, and shortly thereafter he developed aphasia and impairment in vision.

The past family and marital histories were non-contributory.

Physical examination revealed a well-developed and well-nourished, acutely ill, weak, aphasic man. There were slight ptosis and edema of the left upper eyelid, with acute tenderness over the left frontal sinus. The neck was stiff to passive flexion. Because of poor co-operation, a funduscopic examination was impossible. The nose showed acute edema with no pus. The tongue was dry and coated, and there was thick tenacious mucus over the pharynx. Examination of the heart and lungs

was negative. The blood pressure was 120 systolic, 70 diastolic. The bladder was palpated almost at the level of the umbilicus. The neurological examination showed that the patient's eyes moved normally toward the left, but failed to move or follow objects beyond the midline to the right. The pupils were round and equal and reacted to light. Corneal reflexes were present. The remaining cranial-nerve examination was unsatisfactory. The muscles of the right arm and leg were paralyzed, indeed one neurologist diagnosed a right hemiplegia with a right homonymous hemianopsia. The tendon reflexes in the arms were less active on the right side. Knee and ankle jerks were not obtained, and there was no plantar response on either side. There was no reaction to pinprick over the right leg, arm and face, but the left arm and leg were withdrawn when thus stimulated.

The temperature was 104.8°F, the pulse 88 and the respirations 24.

Examination of the blood revealed a red-cell count of 4,200,000 with 82 per cent hemoglobin, and a white-cell count of 29,000 with 80 per cent polymorphonuclears. The urine was negative. The blood Hinton and spinal-fluid Wassermann tests were negative. The blood nonprotein nitrogen was 37 mg per 100 cc. A lumbar puncture showed a clear "yellowish" fluid with normal dynamics, a cell count of 427 per cubic millimeter with 400 polymorphonuclears, a ++ alcohol protein test, a total protein of 186 mg per 100 cc, a sugar of 81 mg and an essentially normal gold-sol curve. Two days later another lumbar tap revealed similar findings, except that the total protein was 258 mg per 100 cc, and the sugar 100 mg.

Roentgenograms of the sinuses showed haziness in the left frontal ethmoid and the left antrum. There was normal aeration of the sinuses on the right, and no definite change in the bones adjacent to the sinuses. Skull plates showed no evidence of increased intracranial pressure.

The patient rapidly became more acutely ill. He developed twitchings of the right side of the face that were occasionally the precursors of generalized convulsions. He was given sodium luminal intravenously, and sulfapyridine intravenously to a blood level of 145 mg per 100 cc. There was severe retching and vomiting. Small subconjunctival hemorrhages appeared in the right eye. The temperature, pulse and respirations rose on the second hospital day to 106°F, 140 and 50 respectively. Convulsions became more frequent, beginning with localized twitching of the right side of the face, and becoming generalized. There was a conjugate deviation of the eyes toward the left,

finding and in nearly every case the cerebral cortex has suffered severe, irreparable damage. These are not abscesses in the true sense. The pus fills a preformed space and is not walled off. In the older cases there is some organization of the exudate next to the dura, but this does not surround the collection of pus.

We find on going over the clinical records that the symptoms and findings generally follow a fairly definite pattern, and we believe that the condition can be diagnosed in a larger proportion of cases than it has been in the past. There is the history of chronic sinus infection or, less often of chronic middle-ear infection, which may have been going on for years. Then, presumably with the beginning of the subdural infection there is severe headache, usually more severe in the early stages on the affected side. The patient is drowsy and looks very ill. The temperature quickly rises to from 103 to 105°F or higher. There is rigidity of the neck. The spinal fluid, which is nearly always under increased pressure (ranging from 190 to 350 mm of water), contains both lymphocytes and polymorphonuclear leukocytes (15 to 1000 per cubic millimeter) and an elevated total protein. The sugar and chlorides are normal and so help to differentiate this condition and a generalized leptomenigitis. Stupor increases and toward the last usually with the onset of deep coma, focal signs appear. The important ones most frequently found are one or more of the following: hemiparesis, hemiplegia, paralysis of contralateral conjugate deviation of the eyes and, in left-sided lesions, aphasia. In most of the cases complicating nasal sinus infection, another very important early sign is swelling about the eye on the affected side. The course is extremely rapid, and death occurs in from five to fifteen days.

The outstanding features which should lead one to suspect subdural abscess are swelling about the eye (in cases with nasal sinus infection), severe lateralized headache, high fever, drowsiness rapidly progressing to stupor, and rigidity of the neck associated with a low or moderately increased cell count in a spinal fluid under elevated pressure in which the sugar and chlorides are normal. With the onset of focal signs one can be reasonably sure of the diagnosis, but by that time the outlook is all but hopeless. It might be possible to save some of these patients if the abscess could be drained before these events develop, or perhaps even at the beginning of this stage. With the help of chemotherapy the outlook ought to be better than it has been in the past. I believe, too, that valuable time should not be lost in operations on sinuses,

myelitis of the frontal bone, mastoids and so forth. These conditions can be dealt with later if the patient recovers after drainage of the abscess.

DR. TOBEY: Was there any generalized meningitis?

DR. KUBIK: The subarachnoid exudate was quite well limited to the area which was covered by the abscess. That is the usual finding, and in most of these cases there is practically no basilar meningitis.

DR. TOBEY: The tooth extraction probably precipitated the whole thing.

DR. RACKELMANN: How do you explain the increased cells in the spinal fluid?

DR. KUBIK: By the localized meningitis beneath the subdural abscess.

### CASE 26352

#### PRESENTATION OF CASE

A fifty-five year-old American Negro painter entered complaining of shortness of breath, diarrhea and vomiting.

Approximately one year before entry the patient had had a slight cold, following which he began to have shortness of breath and a slight cough productive of yellowish white sputum. The ankles became swollen toward evening and improved overnight, although the right foot remained slightly swollen all the time. Seven months before entry he noted that he became fatigued very easily and had palpitation. Three months before admission he began to have watery diarrhea two or three times a day for a few days a week. He also vomited occasionally after meals. Neither the vomitus nor the stools contained blood. At this time his urine was "muddy." The face became swollen occasionally. One week before entry he took some "salts," with moderate relief of the vomiting. The urinary output had decreased, and he had become thirsty. Two days before entry he was somewhat dizzy, his vision was blurred and everything appeared hazy. He had had no chest pain or fever. He had had nocturia once a night for the past four years.

The family and marital histories were non-contributory.

Three and a half years before entry he was in this hospital at which time a bilateral vasectomy and suprapubic cystotomy were performed for an obstructing prostate. At that admission the heart was not enlarged. The blood pressure was 138 systolic, 90 diastolic, the peripheral arteries were sclerosed. There was bilateral exophthalmos. The urine showed a slight trace of albumin and had specific gravities of 1.018 and 1.040. The non-

protein nitrogen ranged between 54 and 88 mg per 100 cc, a renal function test showed 13 per cent excretion of the dye in two hours. One month later he was readmitted to this hospital. A consultant found no cardiac symptoms but considerable edema of the feet. The heart was not enlarged, and no murmurs were heard. The blood pressure on admission was 168 systolic, 110 diastolic. The nonprotein nitrogen of the blood was 48 mg per 100 cc, and the renal function test showed 20 per cent excretion in two hours. The urine had a specific gravity of 1.020. He was given digitalis preoperatively. A suprapubic prostatectomy was performed. The pathological report was "Benign hypertrophy and chronic prostatitis."

Physical examination showed a well-developed and well-nourished man, lying in bed in no apparent discomfort. The breath had a urinous odor. The face and eyelids were puffy. The mucous membranes were pale. The eyes showed exophthalmos, more marked on the right, and myopia. Light perception was present only in the right eye. Both lenses showed opacities. There was marked bilateral chorioretinitis, with retinal atrophy and pigment changes. Inguinal lymph nodes were felt on both sides. Both lungs showed a few moist rales at the bases, with scattered inspiratory and expiratory rhonchi, the breath sounds were rough throughout both lungs. The heart was slightly enlarged to the left, the maximal apical impulse being felt 10.5 cm from the mid-sternal line in the fifth interspace, 10 centimeter beyond the mid-clavicular line. The sounds were of good quality. There was a soft blowing systolic murmur at the apex. The aortic second sound was slightly accentuated. The blood pressure was 178 systolic, 122 diastolic. The peripheral arteries were firm and palpable. There was moderate pitting edema of both feet, ankles and lower legs.

The temperature was 98°F, the pulse 95, and the respirations 22.

Examination of the urine showed specific gravities ranging from 1.008 to 1.015, a large trace of albumin and 10 to 20 white blood cells and 3 to 4 red blood cells per high-power field. The blood showed a red-cell count of 2,700,000 with a hemoglobin of 50 per cent, and a white-cell count of 6700 with 68 per cent polymorphonuclears. A blood Hinton test was negative. The nonprotein nitrogen of the blood was 102 mg per 100 cc, the carbon dioxide combining power 51.6 vol per cent, and the serum protein 5.6 gm per 100 cc, the chlorides were equivalent to 101 cc. of N/10 sodium chloride. The renal function test showed 0

per cent excretion at the end of an hour and fifteen minutes. The stools were negative.

On the second day he had an attack of what was called cardiac asthma. He was in bed when suddenly his lungs became markedly congested. He developed coarse rhonchi, and the blood pressure rose to 300 systolic, 160 diastolic. Blood pressure cuffs were applied to the four extremities, with a pressure of 200 mm of mercury. This produced relief within seven minutes. The patient stated that it was the first attack of this kind that he had ever had. On the third day an apical protodiastolic gallop rhythm was heard. The chest was filled with coarse asthmatic rales, as well as with small fine ones. During the day he had several attacks similar to that on the day before, all relieved by the application of blood pressure cuffs. He continued to have these attacks and died on the fifth day in an attack of acute pulmonary edema.

#### DIFFERENTIAL DIAGNOSIS

DR ROBERT E. GLENDY. It is apparent from the antecedent history that three and a half years before his final admission to the hospital this man had had uremia as a result of urinary suppression from prostatic disease, which, according to the pathological report following prostatectomy, was attributable to benign hypertrophy and chronic prostatitis. There was evidence of considerable impairment of renal function, including albuminuria, poor excretion of dye and nitrogen retention in the blood. The blood pressure was high (168 systolic, 110 diastolic) before prostatectomy. In view of the hypertension it is fair to assume that he had had chronic prostatic obstruction over a rather prolonged period before seeking relief. It is very likely also that because of back pressure due to the obstructing prostate the kidneys were permanently dilated and irreparable damage had been done to the renal parenchyma (atrophy and perhaps some infection). The elevated blood pressure, no doubt present for some time before prostatectomy, must have resulted in a certain amount of cardiac strain, but no cardiac enlargement or other evidence of cardiac disability was recorded at this time, although he was given digitalis preoperatively, perhaps as a precautionary measure. The marked edema of the feet was probably renal in origin from retention of water and salts and possibly a low serum protein. The peripheral arteries were said to be sclerosed, but this fact does not necessarily bear any direct relation to the condition of the arteries elsewhere, since mild to moderate degrees of peripheral arteriosclerosis are not uncommon at this age. Bilateral exophthalmos was observed at both hos-

pital admissions but presumably was not related to the illnesses described here.

The past medical history reveals that he had had erysipelas in early life. One might speculate about the possibility of a complicating nephritis with some early renal impairment, but this is such a far cry that it hardly deserves mention. Because of the exposure to lead as a painter I wonder about chronic lead poisoning as a possible factor, at least in the production of the degenerative changes—arteriosclerosis and interstitial nephritis with hypertension—that are so often present in the late stages of this condition. In the absence of other manifestations of lead poisoning we can go no farther than to consider it as a possible contributing factor. The history of pleurisy at the age of twenty-one does not seem to fit into this picture anywhere.

Except for the statement that he had had nocturia we have no information about the state of his health for some two and a half years following the prostatectomy. Then one year before entry the signs and symptoms of his final illness began. They were ushered in by a cold, which not uncommonly precipitates or aggravates cardiovascular symptoms. The dyspnea, cough and swelling of the ankles noted toward evening undoubtedly represent the end result of long standing myocardial strain from arterial hypertension, manifesting itself in a diminished cardiac reserve with some gross evidences of failure. These symptoms increased as time went on, and to them were added others, namely, easy fatigue and pallor. The diarrhea, vomiting, decrease in urinary output, swelling of the face, dizziness and disturbance in vision that developed during the three months prior to entry all point to advancing renal failure which, I believe, is the underlying factor behind the whole picture. The "muddy" urine might be expected with the decreased urinary output, and also suggests that there was some infection in the urinary tract. The absence of fever, however, is against an acute infection, at least one of much importance. The mechanism behind the gastrointestinal symptoms may have been local edema of the viscera or uremic toxemia or both. Finally, the dizziness and disturbance of vision suggest cerebral edema and vascular lesions in the optic fundi, respectively.

These assumptions from the history find confirmation in the physical findings. The uninfused breath, puffy face and eyelids, pallor of the mucous membranes, retinal changes, hypertension, cardiac enlargement, pulmonary congestion and peripheral edema are altogether typical of cardiovascular disease. I presume that the changes in the

optic fundi were described as chorioretinitis simply because the choroid was prominently implicated. The myopia may have contributed to this, but with retinal atrophy the choroidal vessels naturally become more easily visible. Opacities of the lenses were additional factors in his failing vision. The systolic murmur at the cardiac apex was probably due to dilatation of the left ventricle, with functional mitral regurgitation.

The laboratory studies showed a urine containing a large amount of albumin and cellular elements consistent with both chronic nephritis and some mild infection anywhere along the urinary tract. Casts were conspicuous by their absence. This seemed to merit more than passing consideration, so I asked that this be confirmed before going farther with the case, and I was assured that no casts were present. Assuming this to be an accurate observation we therefore have some evidence to support the idea that the renal failure resulted from the earlier effects of prostatic obstruction plus some chronic infection rather than from nephritis of non surgical origin. The absence of casts is rather the rule than the exception in surgical nephritis. The ability of the kidneys even at that late date to concentrate the urine to 1015 also favors surgical nephritis in which the remaining functioning cells undergo compensatory changes in size and function that are not encountered in other types of nephritis. The anemia, nitrogen retention and lowered serum protein are all consistent with the picture of renal failure, which is quite apparent also from the inability of the kidneys to excrete the dye used in the renal function test. The carbon dioxide combining power of the blood was at the lower limit of normal. With such marked impairment of kidney function one would expect it to be lower.

From the account of the last few days of his life it is apparent that he died of myocardial failure, when his heart could no longer compensate for the strain imposed upon it by the marked elevation of blood pressure. This, I believe, was secondary to the underlying renal disease.

In summarizing the whole situation the sequence of events seems to have been prostatic obstruction with back pressure, infection and more or less permanent damage to the renal parenchyma with some temporary relief following prostatectomy. The renal damage was probably perpetuated by chronic infection. Hypertension and cardiac hypertrophy subsequently became a prominent part of the picture as the renal impairment advanced, and he finally succumbed to renal and cardiac failure.

My prediction is that the kidneys showed pro-



nounced atrophic changes in the parenchyma, along with arteriolar and capillary changes of a diffuse nature. The kidney pelves and calyces may have shown evidence of the old prostatic obstruction. Judging from the urinary findings, blood counts and temperature there was probably not much evidence of recent purulent infection in the urinary tract, although infection undoubtedly contributed to the impairment of renal function over the period of years. The heart was undoubtedly dilated and hypertrophied, with preponderant enlargement of the left ventricle, and the lungs waterlogged.

#### CLINICAL DIAGNOSES

Chronic glomerular nephritis, with hypertension and hypertensive heart disease.  
Uremia  
Cardiac asthma

#### DR. GLENDY'S DIAGNOSES

Chronic pyelonephritis, with atrophic and inflammatory, arteriolar and capillary lesions  
Hydronephrosis  
Hypertensive heart disease.  
Marked cardiac enlargement  
Congestive heart failure  
Pulmonary edema

#### ANATOMICAL DIAGNOSES

Pyelonephritic atrophy of the kidneys (healed pyelonephritis)  
Hypertrophy of the heart  
Pulmonary edema

Chronic passive congestion, slight  
Arteriosclerosis, cerebral  
Operative wound suprapubic prostatectomy

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY. As Dr. Glendy predicted, this patient showed atrophic kidneys, hypertrophied heart and wet edematous lung. The systemic arterial system, including the coronary arteries, showed remarkably little arteriosclerosis, but the small arteries and arterioles of the brain were, in contrast, rather markedly involved. The interest of the anatomical diagnosis lies in the nature of the renal lesion. There was no gross dilatation of the renal pelves, and the renal cortices were diffusely rather than focally scarred, so that a gross diagnosis of pyelonephritis was not suggested. On microscopic examination, however, several findings which have recently been emphasized by Weiss and Parker\* point to a pyelonephritic atrophy. There are great numbers of completely hyalinized glomerular tufts, with usually marked periglomerular fibrosis. There is disproportionate tubular destruction, and definite increase of interstitial fibrous tissue, with considerable lymphocytic infiltration but no evidence of acute infection. Many of the tubules contain the dense so-called "colloid" casts. The blood vessels show very marked intimal proliferation. The histological criteria, therefore, appear to substantiate completely Dr. Glendy's diagnoses.

\*Weiss S. and Parker F. Jr.: Pyelonephritis: its relation to vascular lesions and to arterial hypertension. *Medicine* 18:221-315, 1939.

# The New England Journal of Medicine

Formerly the  
Boston Medical and Surgical Journal  
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND  
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE  
ON PUBLICATIONS

Official Organ of

THE MASSACHUSETTS MEDICAL SOCIETY  
THE NEW HAMPSHIRE MEDICAL SOCIETY  
THE VERMONT STATE MEDICAL SOCIETY

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**NOTICE:** For early publication should be received not later than noon on Saturday.

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## MEDICAL PREPAREDNESS INDUSTRIAL MEDICINE

As already stated editorially, an unexcelled efficiency of machines is but of little advantage to preparedness if the production of war supplies is hampered by a physical breakdown of those who man them. Hence, any scheme to further national defense should include elaborate plans for the protection of the worker and his family.

The broader aspects of the problem have to do with the health of the nation as a whole, and as previously noted, include an improved nutritional status, the correction of remediable defects and the application of approved procedures of preventive medicine. But the protection of the skilled worker — of whom there is acknowledged to be a serious shortage, — as well as that of apprentices who are now employed or who may eventually replace those called into active service, demands the intelligent application of present-day knowl-

edge concerning industrial medicine. This is particularly true in those industries that are forced to expand by leaps and bounds new hazards are sure to occur, and there is certain to be relatively less protection against those that have long been recognized. Adequate preventive measures must be instituted, and those who are injured or become ill while employed must receive the best of medical and nursing care.

In the past twenty five years, the art and science of industrial medicine have rapidly advanced, largely through the impetus afforded by private industry, when, as the handicap caused by the loss of working time by indispensable workers began to be appreciated, it took steps to protect the health of its employees. This branch of medicine is now a well recognized and well justified specialty, and more and more physicians have become interested in it, on either a part-time or full-time basis. Instruction can be obtained in certain medical schools or schools of public health, and federal and state agencies are maintained to assist in solving whatever problems arise. The Council on Industrial Health of the American Medical Association has recently become quite active, and through its efforts, committees on industrial health have been organized among the state medical societies within the past two years. All these facilities are available, but they must be augmented if the challenge offered by potentially tremendous industrial expansion is to be properly met. An increase in trained personnel is needed, and the Committee on Medical Preparedness of the American Medical Association has recently recommended to the National Defense Commission "that the necessary funds be furnished to the U S Public Health Service to provide the training of physicians, chemists, mechanical engineers and other professional personnel in order to cope with the industrial hygiene problem in the present national emergency."

## FIVE-DAY TREATMENT OF SYPHILIS

ERLICH's vision of a one-dose method of treating syphilis has been revived. At a recent conference in New York City a report<sup>1</sup> was given of the so-called "five-day treatment of syphilis" using arsphenamine preparations highly

nounced atrophic changes in the parenchyma, along with arteriolar and capillary changes of a diffuse nature. The kidney pelves and calyces may have shown evidence of the old prostatic obstruction. Judging from the urinary findings, blood counts and temperature there was probably not much evidence of recent purulent infection in the urinary tract, although infection undoubtedly contributed to the impairment of renal function over the period of years. The heart was undoubtedly dilated and hypertrophied, with preponderant enlargement of the left ventricle, and the lungs waterlogged.

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1939, making the expected date of confinement May 11

The patient was first examined in the office on September 29, 1939, at which time all physical findings were normal and the uterus was definitely enlarged, with slight softening of the anterior wall. The pregnancy was uneventful except for a slight cold and cough for one week before hospital entry.

Within one to two hours after admission to the hospital she developed a severe hacking cough, which was painful, and raised some sputum, which was slightly bloody. As she presented the typical picture of an acute lobar pneumonia, she was seen by an internist. The temperature was 102°F., the pulse 120, and the respirations 25. The left chest was splinted, motion, cough and deep breathing were all painful, and the pain was referred largely to the region of the left clavicle. Examination revealed the throat red and dry, the tongue slightly coated. There were no palpable lymph nodes. The lungs showed decreased resonance and breathing over the whole left chest, particularly posteriorly, and a friction rub in the left axilla. There were no definite rales or changes in breathing. The right lung was clear throughout. The heart sounds were rapid but otherwise normal. The abdomen was increased in size to that of an eight months pregnancy. There was no costovertebral tenderness. A diagnosis of lobar pneumonia, probably in the left lower lobe, was made. As there was no portable x-ray equipment available, no films were taken. A typing reported less than nine hours after the onset of the disease, showed Type 7 pneumococcus. In view of the fact that the patient was known to be allergic, serum was not given and sulfapyridine was started—30 gr immediately, 30 gr in two hours, and then 15 gr every four hours. She was given 1/6 gr of morphine subcutaneously, and a chest swathe was applied. The hemoglobin was 84 per cent (Sahli), the red-cell count 4,050,000, and the white-cell count 25,100. A blood culture taken before the medication was started showed a Type 7 pneumococcus.

In twelve hours the temperature had dropped to 100°F., but the patient was still somewhat toxic. The signs in the chest were fairly well localized in the left base, with dullness in the axilla and a little posteriorly. There were a few crackling rales over this area, with the friction rub still present but less marked. The patient was nauseated from the sulfapyridine.

On April 5 she began to look much better. The signs in the lungs started to clear, and the breath sounds came through better, being

slightly bronchial. The rales were more obscure in the upper part of the left lobe. Sulfapyridine was then given every six hours. The hemoglobin had dropped to 66 per cent (Sahli), and the red-cell count to 3,430,000. From this time on, the patient made rapid progress and the lungs cleared rapidly. She was moved by ambulance to another hospital, where more satisfactory nursing care could be arranged. Ten days after the onset of the infection, x-ray films showed the lungs to be clear, and the patient was discharged home on the twelfth day.

Two weeks later, the patient started in labor and was delivered of a normal male child. She remained in the hospital for sixteen days and had a normal puerperium.

*Comment.* This case illustrates proper treatment and an ideal result. Chemotherapy appears to be as effective in cases of pneumonia in pregnancy as it is in uncomplicated pneumonia, and early hospitalization, early consultation, early typing and early chemotherapy may reduce the mortality of pneumonia during pregnancy to such a level that its inherited fear will be dispelled.

## DEATHS

JENKINS—THOMAS L. JENKINS, M.D. of Topsfield, died July 29. He was in his seventy-fifth year.

Dr. Jenkins received his degree from Harvard Medical School in 1890 and was a fellow of the Massachusetts Medical Society and the American Medical Association. During the World War he was a senior surgical officer of the American Expeditionary Force.

THORNDIKE—AUGUSTUS THORNDIKE, M.D., of Boston, died August 23. He was in his seventy-eighth year.

Born in Paris, France, he attended Noble's School in Boston and Harvard College. He received his degree from the Harvard Medical School in 1888 and served as house officer and intern at the House of the Good Samaritan, the Massachusetts General Hospital and the Boston Lying-in Hospital. Dr. Thorndike was associated with the Boston Dispensary until 1895, serving consecutively as assistant district physician, orthopedic surgeon and surgeon. He had also served as visiting physician at St. Luke's Home for Convalescents and the House of the Good Samaritan and assistant surgeon at the Children's Hospital in Boston. From 1907 to 1917 he was a member of the Department of Orthopedic Surgery at the Harvard Medical School.

He was a member of the Massachusetts Medical Society and the American Medical Association and a fellow of the American College of Surgeons. He also held memberships in the Massachusetts Medical Benevolent Society, Boston Society of Medical Sciences and Boston Medical Library.

His sons, Dr. Augustus Thorndike, Jr., Robert and Charles, and his daughters, Alice and Mary survive him.

## CORRESPONDENCE

### LICENSING OF ALIEN PHYSICIANS

To the Editor I have just finished reading the editorial, "Aliens and the Practice of Medicine." When I took the state examinations last November I was struck by the number of refugees in the examination rooms. They were of all ages, varying from a quiet, elderly man, who evidently had been a teacher in his native land, judging from the number of young people who clustered around him between examinations, to a young girl, who became hysterical on observing one of the examinations.

Rather than judging this hodge-podge *en masse* I believe it would be better to individualize treatment. Let the president of the Massachusetts Medical Society appoint a committee to examine them and their credentials, so as to make recommendations to the Board of Registration in Medicine as to whether they would be better fitted to (a) study longer in an American medical school, (b) intern for a year in an American hospital, (c) take the examinations for practice or (d) be admitted to practice without examination, presumably to continue a specialty or become a teacher in a medical school.

I think such a plan as this would protect the public from incapable practitioners and would not place the refugee in a position untenable to him. By doing this the medical profession will assume a responsible position in this problem.

JOSEPH A. BRADLEY, M.D.

215 Haverhill Street,  
Lawrence, Massachusetts

By statute the licensing of physicians is a function of the Board of Registration in Medicine, and the procedure employed in determining the fitness of candidates is also defined by law. While Dr. Bradley's suggestion is reasonable, the participation of the Massachusetts Medical Society in determining the qualifications of candidates would necessitate additional legislative action. Ed

## REPORTS OF MEETINGS

### BOYLSTON MEDICAL SOCIETY

At the Harvard Medical School on May 5, the Boylston Medical Society presented Professor Charles H. Best, of the University of Toronto, who spoke on "Factors Influencing the Production and Liberation of Insulin from the Pancreas."

The effects of various diets and of starvation on the insulin content were first considered. The smallest amounts of insulin were extracted from rats either starved or fed solely on fat. These animals showed a glucose tolerance curve simulating a diabetic curve, which indicates that the rate of release of insulin, as well as the total amount, is diminished under these dietary conditions. Microscopic examination of the islet cells in such animals, however, failed to reveal any notable changes indicative of degeneration. Finally, it was noted that recovery from this depressed state of insulin production was best accomplished by a balanced diet. Rats fed on high fat diets showed smaller quantities of insulin than did similar animals on an equicaloric carbohydrate diet. Prolonged experiments on high-carbohydrate and fat diets failed to show such striking variations from normal.

Newer investigations on the effect of insulin on normal as well as on fat-fed and starved rats reveal that the use of this hormone further depresses the production of insulin

from the pancreas and suggest that all these procedures are measures to cause a reversible "atrophy of disuse" in the islet cells. The apparent diabetic glucose-tolerance curve, therefore, is really an indication of a resting state, which is evidenced by the gradual resumption of the usual production when the normal diet without insulin is initiated. This finding was held to elucidate the diabetic-tolerance curve observed in tumors of the islet cells which oversecrete hormone and consequently depress production by normal tissue, which then responds only sluggishly, if at all, to carbohydrate stimulation. It also explains the findings in the insulin treatment of dementia praecox.

In order to investigate the effect of the diabetogenic extract of the anterior pituitary gland, as used by Houssay to produce transient, and by Young to produce permanent diabetes, Best and his collaborators removed the pancreas of animals treated by the Young method and found no increase in the intensity of the disease. Young had reported changes in the pancreas, and Best and his collaborators found a decrease of insulin content. It was suggested, therefore, that the pancreas is the intermediary whereby the hypophysis exerts its effect. Furthermore, the islet cells reveal no evidence of recovery in permanent pituitary diabetes in the dog.

Preliminary results of some recent studies demonstrate that the administration of insulin prevents the production of permanent pituitary diabetes in susceptible animals, that no degenerative changes, except proliferation, were brought about in the pancreas, and that no marked diminution of insulin content occurred.

Dr. Best concluded that starvation, a fat diet or the administration of insulin rests the islet cells and protects them from the effects of the diabetogenic hormone of the anterior pituitary gland. Possible clinical application of these facts was suggested in order to rest the islet cells from the possible deleterious effects of the pituitary gland in a susceptible person. A diet low in calories, low in carbohydrate or high in fat, with or without the addition of insulin, may be prescribed. If stimulation is desired subsequently, a high-carbohydrate diet may be employed, with insulin used for protection. This procedure supports the early views of Allen to the effect that the islet cells are capable of protection by proper diets. A difficult clinical experiment, the observation of 1000 children with a family history of diabetes rested by diet (and insulin) and 1000 controlled cases for the incidence of subsequent diabetes, was suggested.

### ALPHA OMEGA ALPHA

At the Harvard Medical School on May 15, the Harvard Chapter of Alpha Omega Alpha presented Professor Robley Evans, of the Massachusetts Institute of Technology, who spoke on "Some Medical Applications of Radioactivity."

A review of the physical aspects of radioactivity was given, and the statement was made that any competent cyclotron today is capable of producing more radioactivity than all the radium in the world. Every known chemical substance has now been transmuted by this method. Dr. Evans pointed out that artificial radioactive compounds are actually "spies" rather than "tracers," for they are indistinguishable from the natural element in ordinary mixtures.

In indicating some of the applications of radioactivity to medicine, Dr. Evans ranked it in importance with the microscope and roentgen rays. One use of radioactivity has been in the study of iodine metabolism carried on by

the combined physician-physicist team of Drs. Means, Hertz, Roberts and Evans. It has revealed that this element, and not all halogens are selectively concentrated by the thyroid gland. The greatest collection of circulating iodine occurs in the first ten to fifteen minutes. It is especially marked in pregnancy and hyperplasia of any sort. In fact the iodine accumulation by the thyroid gland is seventy times that expected if a general diffusion had taken place. Hyperplasia from cyanide and cabbage ingestion in rabbits causes a differently shaped although grossly similar, curve of accumulation. Due to the fact that the greatest amount of iodine is concentrated in the thyroid gland after the first dose of iodine, it was considered possible that a single dose of potassium iodide might serve as well as repeated ones in the treatment of hyperplastic thyroid disease in man. Preliminary reports on this work indicate that this is actually the case, at least in certain persons.

## NOTICES

### ANNOUNCEMENT

JOHN J. SLATTERY M.D., announces the removal of his office, effective September 1 1940 from 95 to 89 Mt. Auburn Street, Watertown.

### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly staff meeting of the New England Hospital for Women and Children will be held in the classroom of the nurses residence on Thursday, September 5 at 7:15 p.m. The subject will be "Clinicopathological Reports on Two Cases with Pancreatic Disease." Dr. Gullis Lindh Muller will preside.

### SOCIETY MEETINGS AND CONFERENCES

- SEPTEMBER 2-6—American Congress of Physical Therapy Page 862, issue of May 16.
- SEPTEMBER 5—New England Hospital for Women and Children. Nocke above.
- SEPTEMBER 12-14 May 8—Preston Association of Physicians Page 263 issue of August 15.
- SEPTEMBER 16—New England Society of Anesthesiology Page 305 issue of August 22.
- SEPTEMBER 16-20—American Occupational Therapy Association Page 263, issue of August 15.
- SEPTEMBER 17-19—Clinical Congress of the Connecticut State Medical Society. Page 305 issue of August 22.
- OCTOBER 6-11—Annual meeting of the American Academy of Ophthalmology and Otorhinolaryngology Page 81 issue of July 11.
- OCTOBER 8-11—American Public Health Association. Page 655 issue of April 11.
- OCTOBER 11, 12—Pa American Congress of Ophthalmology Page 858 issue of May 23.
- OCTOBER 14-25—1940 Graduate Fortnight of the New York Academy of Medicine. Page 305 issue of August 22.
- OCTOBER 21—American Board of Internal Medicine. Page 369 issue of February 29.
- JANUARY 4 1941—American Board of Obstetrics and Gynecology Page 364, issue of June 20.
- MARCH 8—American Board of Ophthalmology Page 201 issue of August 1.
- APRIL 21-25—American College of Physicians. Page 1065 issue of June 20.

### DISTRICT MEDICAL SOCIETY

#### RETROK

- SEPTEMBER 7—Cancers meeting Page 305 issue of August 22.

### BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

*Synopsis of the Principles of Surgery* By Jacob K. Beriman A.B., M.D., assistant professor of surgery Indiana University School of Medicine, Indianapolis. 12 cloth, 615 pp., with 274 illustrations. St. Louis C. V. Mosby Company 1940 \$5.00

*The Bacteriology of Public Health* By George M. Cameron, Ph.D., associate professor of bacteriology University of Tennessee. 8 cloth, 451 pp., with 35 illustrations and 8 color plates. St. Louis C. V. Mosby Company 1940. \$3.50.

*The Emperor's Lick The legend concerning Napoleon's affliction with scabies* By Reuben Friedman, M.D., assistant professor of dermatology and syphilology Temple University School of Medicine, Philadelphia 8 cloth 82 pp., with 10 illustrations. New York. Froben Press 1940 \$1.50

*Manual of Medical and Surgical Emergencies* Edited by J. C. Geiger M.D., director, Department of Public Health City and County of San Francisco, California. 8 cloth 199 pp. San Francisco J. W. Stacey Inc. \$2.50

*Legal Guide for American Hospitals Prepared in collaboration with the Council on Government Relations of the American Hospital Association.* By Emanuel Hayt, LL.B., and Lillian R. Hayt, M.A., J.D., of the New York Bar 8 cloth 608 pp. New York Hospital Textbook Company 1940. \$5.00.

*American Doctors of Destiny A collection of historical narratives of the lives of great American physicians and surgeons whose service to the nation and the world has transcended the scope of their profession.* By Frank J. Jirka M.D., with an introduction by Harold W. Camp. 8 cloth 361 pp., with 20 portraits by Raymond Warren. Chicago Normandie House, 1940. \$3.75

*Dynamics of Inflammation An inquiry into the mechanism of infectious processes* By Valy Menkin, M.D., instructor Department of Pathology Harvard Medical School 8 cloth 244 pp., with 50 illustrations and 27 tables. New York Macmillan Company 1940. \$4.50

*Observations Made during the Epidemic of Measles on the Faroe Islands in the Year 1846* By Peter Ludvig Panum M.D., and translated from the Danish by Ada Sommer ville Hatcher with a biographical memoir by Julius Jacob Petersen, M.D., translated from the Danish by Joseph Dumont, and an introduction by James Angus Doull, M.D. 8 cloth, 111 pp. New York Delta Omega Society (distributed by the American Public Health Association) 1940 \$2.50

*La maladie de Bernier-Boeck-Schaumann ses manifestations cutanées ganglionnaires pulmonaires osseuses oculaires glandulaires viscérales nasales nerveuses—une nouvelle grande réticulo-endothéliose* By L. M. Pautrier clinical professor of dermatology and syphilology Faculty of Medicine, Strasbourg 4 paper 341 pp., with 105 illustrations. Paris Masson et Cie. \$2.05

*The International Medical Annual A year book of treatment and practitioners index (1940)* Edited by H. Letheby Tidy M.A., M.D. (Oxon.) F.R.C.P., and A. Rendle Short, M.D., B.Sc., F.R.C.S. 8 cloth 545 pp.

with 65 plates Baltimore Williams & Wilkins Company, 1940 \$6 00

*Influence of a Public Health Program on a Rural Community Fifteen years in Rutherford County, Tennessee, 1924-1938* By W. Frank Walker, Dr. P. H., and Carolina R. Randolph 12°, paper, 106 pp., with 46 tables and 6 charts New York The Commonwealth Fund, 1940 25 cents

*As I Remember Him The biography of R. S.* By Hans Zinsser, M.D., S.D. 8°, cloth, 443 pp. Boston Little, Brown & Company, 1940 \$2 75

*Frank Howard Lahey Birthday volume (June 1, 1940)* 8°, cloth, 466 pp., with 71 illustrations and 29 tables Springfield, Illinois Charles C. Thomas, 1940 Privately printed

## BOOK REVIEWS

*Treatment of War Wounds and Fractures* By J. Trueta, M.D. 12°, cloth, 146 pp., with 48 illustrations New York Paul B. Hoeber, Inc., 1940 \$2.50

The author of this volume took a very active part in caring for military and civilian casualties of the late Spanish civil war. From this large experience he concludes that the closed method is by all odds the best treatment for compound fractures. In the United States this therapy has found its widest use in chronic osteomyelitis under the name of "Orr treatment." It consists essentially of thorough debridement, packing of the wound, reduction of the fracture and application of an unpadded plaster cast without a window. When soft tissue damage is slight, as with a small bullet wound, the packing may be omitted. The early use of this treatment in compound fractures lowers the incidence of serious sepsis, hastens healing and facilitates transportation to hospitals far from the scene of the first treatment.

Of 1073 cases treated by this method, 976 showed good or satisfactory results, there were only 6 deaths. Trueta does not give exact figures for non-union, but he leaves the reader to understand that the number is smaller than that with other methods of treatment.

The problems of individual fractures in both extremities are enumerated, and many representative cases are discussed. There are good illustrations and photographs of the cases. This work has received much favorable attention and deservedly so, for it should help to reduce the mortality and morbidity of these common injuries both in war and in peace.

*The Medical Career and Other Papers* By Harvey Cushing 8°, cloth, 302 pp. Boston Little, Brown & Company, 1940 \$2 50

In 1928, Dr. Cushing published a group of his papers in a book entitled *Consecratio Medici and Other Papers* (Boston Little, Brown & Company). Toward the end of his life, he assembled another series of papers on general medical topics, which he had arranged to be published in book form. Since his death in 1939, this task has been carried out by his official biographer, Professor John F. Fulton, of Yale University School of Medicine. The volume contains the reprinting of seven important papers, with the addition of nine biographical sketches. To all readers of the *Journal*, these works of Dr. Cushing are undoubtedly familiar. Some were read in Boston, and many were printed in the *Journal*. It is pleasant to reread them, however, in their present form, and one finds a delightful sense of satisfaction in again visualizing the

principles so skillfully depicted by Dr. Cushing's classmen. No one in recent years has been able to draw such succinct sketches of his contemporaries, nor write with such great brilliance as well as lucidity of style about the old figures of medicine in the past. Moreover, as a reviewer of medicine, particularly as it applied to his own specialty of neurosurgery, Dr. Cushing had no peer. *The Medical Career* is a welcome addition to modern literature, it should be widely read and reread by the present generation and by those to come.

*Fundamentals of Biochemistry* By T. R. Parsons, B.Sc., M.A. Sixth ed. 12°, cloth, 461 pp. Baltimore William Wood & Company, 1939 \$3 00

Because it does not fulfill the requirements of present-day biochemistry and because it is filled with inaccuracies, the sixth edition of this book is a characterless one. The author himself summarizes this fault in his foreword wherein he states "It has been my desire that any merit my book may possess may result from its containing less of information rather than more than other books contain. But I am fully aware that my anxiety for the omission of detail must have run to such excess as to constitute a fault rather than a virtue." Because the mental connecting rods have been left out in explaining certain biochemical processes, the reader is often perplexed and fails to understand the exact situation. This being the case, the reviewer believes that the book is inadequate for instructive purposes as knowledge depends primarily on understanding rather than memory.

*The Rockefeller Institute for Medical Research Studies from the Rockefeller Institute for Medical Research* Vol. 114 8°, paper, 640 pp. Baltimore Waverly Press, 1940 \$2 00

The usual wide range of material is presented. Of special interest is the report of Dubos and others on a bactericidal agent extracted from soil bacteria. The article by Erf and Rhoads on benzol poisoning is of value.

*A Handbook of Accepted Remedies, Symptoms and Treatment of Poisoning* Edited by P. J. Hanzlik, M.D. 12°, paper, 127 pp. San Francisco Department of Public Health, 1940

In 1936, Dr. J. C. Geiger, director of public health, San Francisco, appointed a committee, consisting of five authorities in the fields of public health and pharmacology, for the purpose of preparing a handbook that would contain facts concerning quantitative data and details of miscellaneous procedure incident to the application to and solution of medical problems.

Beginning with the educational features of this brochure, lists of the approved drugs and methods of treatment of the disorders of the several systems of the human body are presented, and following these, sections dealing with vaccines, serums, bioassays, drugs subject to federal regulation, vitamins, foods, symptoms and treatment of poisoning, common emergencies, physiological and pathological data, diagnostic and other tests and so forth, all are set forth in concise language and logical sequence.

The especial reason for the compilation of these lists of useful agents is because of the accepted fact that few people are endowed with the requisite mental capacity to have immediately available all useful knowledge pertaining to medical problems. Although designed especially for hospital staffs, most practitioners will find it a useful and handy reference book.

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NUMBER 10

## JOHN H CRANDON, M.D.† CHARLES C LUND, M.D.,† AND DAVID B DILL, PH.D.§

BOSTON

In other communications<sup>15, 16</sup> we have presented

### EXPERIMENTAL DATA

The white-cell-platelet ascorbic acid, as determined by Butler and Cushman by their own method fell gradually from a relatively normal level of 28 mg per 100 cc. on the seventeenth day of the diet to 4 mg per 100 cc. on the eighty-second day after which the level remained at 3.50.

1210. For the first two months well-cooked meat (not over 200 gm per day) and small amounts of cream were allowed, but thereafter 11 meat and cream were no longer permitted. For the following four months the diet consisted of cereals (wheat, rice, barley), bread, crackers, eggs, beer (not over 50 cc per day), soft drinks (sodas), fruit, vegetables, and milk (not over 500 cc per week). black coffee and standard brand of pure hocolate candy consisting only of chocolate bars and sugar were permitted. For the last two months of the study the diet was a rather dietary period the at 215% for seventy two hours.

1211. Subject received daily 30,000 international unit of Isotrel A, 132 international unit of vitamin B<sub>12</sub>, 30,000 international unit of vitamin A, fortified by 100 Harsco yeast tablets, 50 mg nicotinic acid, 5780 international units of vitamin D<sub>2</sub> oil, after the second month, 4 cc. of whole-germ oil.

<sup>97</sup>From the Fifth Surgical Service and the Surgical Research Laboratory, Boston City Hospital, the Department of Surgery, Harvard Medical School and the Pathologic Laboratory, Harvard School of Business Administration. This work was aided by anonymous donors and Hoffman-La Roche, Inc., New Jersey. Assistance in securing the data was in part furnished by the personnel of the Work Projects Administration (Project 17580).

Harvard professor of surgery, Harvard Medical School; assistant chief  
of surgery, Boston City Hospital.

Professor of Industrial physiology Harvard School of Public Health  
consulting physiologist, Hygiene Department, Harvard University



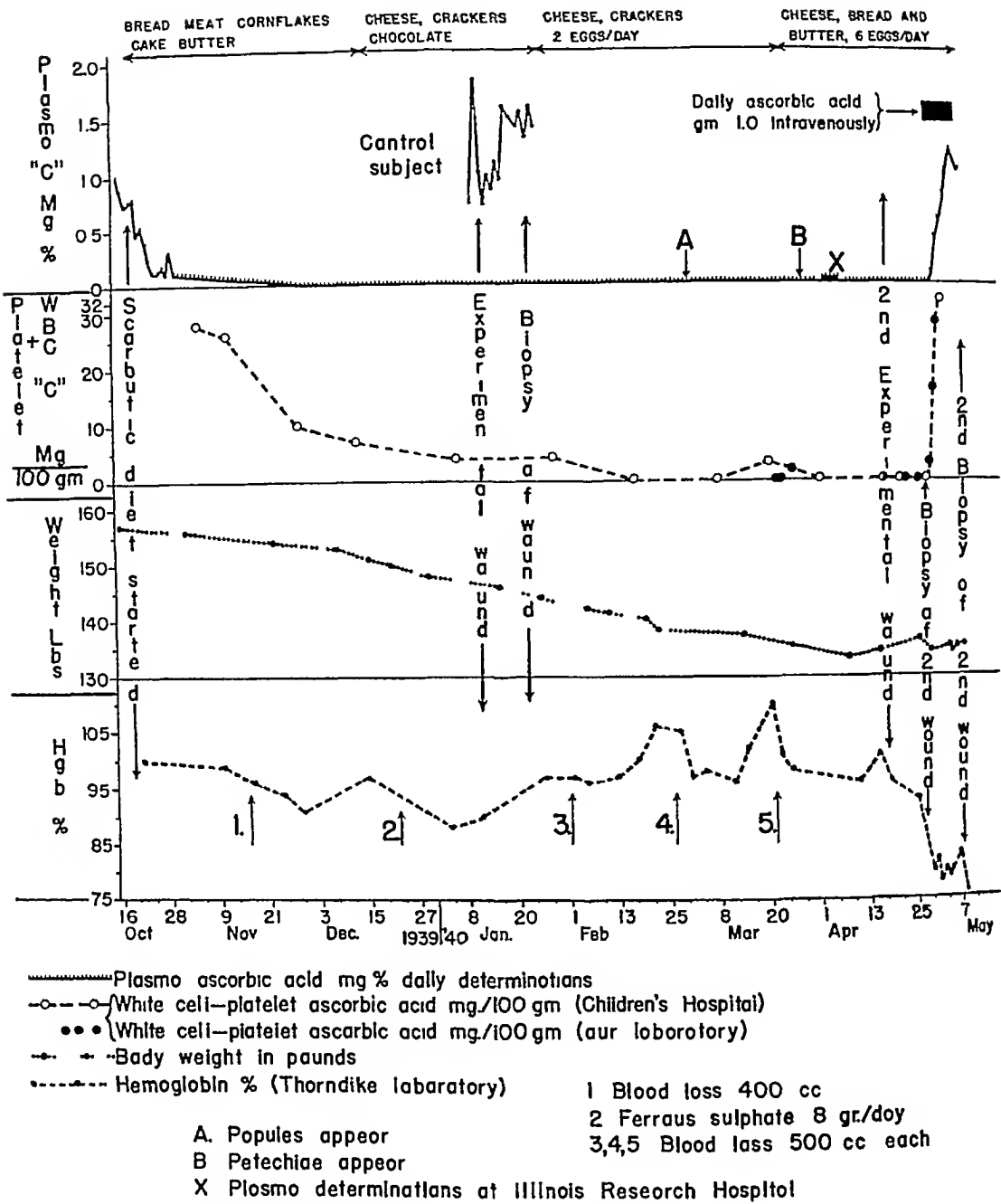


FIGURE 1 Graph of Pertinent Data in a Case of Experimental Human Scurvy

ADDITIONAL DATA

Vitamin C Content of Plasma\* (mg per 100 cc) (17)† 0.2, (23) 0.1, (41) 0.0, (55) 0.0, (79) 0.0, (87) 0.0, (100) 0.0, (121) 0.0, (135) 0.0, (153) 0.0, (181) 0.0, (185) 0.0, (192) 0.0

Vitamin C Content of Whole Blood\* (mg per 100 cc) (17) 0.2, (23) 0.1, (41) 0.1, (79) 0.1, (87) 0.0, 0.0 thereafter, as plasma above

Basal Metabolic Rate (per cent) (1) +11.5, (7) +5.1, (10) +0.9, (13) -12.5, (17) -12.6, (23) -10.7, (30) -5.0, (36) -8.7, (44) -6.2, (48) -14.1, (51) -16.6, (59) -6.4, (70) -20.0, (77) -21.0, (82) -19.6, (89) -9.2, (93) -13.6, (105) -10.3, (110) -10.0, (114) -15.4, (118) -11.0, (133) -8.3, (139) -17.0, (150) -15.9, (156) -15.9, (161) -22.0, (175) -21.8, (181) -17.4, (187) -6.4, thereafter see Table 3

Red-Cell Count (millions) (0) 5.0, (5) 5.0, (12) 5.0, (23) 5.0, (29) donor for transfusion, 400 cc, (30) 4.6, (37) 4.2, (42) 4.5, (57) 4.8, (77) 4.3, (85) 4.5, (102) 5.0, (106) donor for transfusion, 500 cc, (110) 4.9, (122) 5.5, (124) 5.6, (131) donor for transfusion, 500 cc, (132) 5.3, (138) 5.1, (148) 5.4, (156) 5.2, (158) acute blood loss, 500 cc, (159) 5.2, (175) 5.2, (185) 5.2, (190) 4.8, †, (194) 4.2, (195) 4.3, (196) 4.2, (197) 4.3, (198) 4.3, (201) 4.2, (203) 3.8, (205) 4.3, (209) 4.5

White Cell Count (thousands) (0) 4.7, (57) 4.8, (85) 4.5, (102) 4.2, (124) 4.3, (132) 3.5, (138) 4.4, (156) 3.2, (175) 3.4, (180) 3.6, †, (193) 5.0, (195) 4.7, (197) 3.7, (198) 5.4, (201) 9.0, (205) 6.0

During the first four months of the deficient diet all physical findings were negative. There was a slight fall in weight and basal metabolic rate and a feeling of easy fatigability and slight weakness (see below).

tion of hairs. These lesions which progressed in severity during the ensuing three weeks resembled a mild form of the lesion described as typical of vitamin A deficiency<sup>10</sup>. Each papule contained an ingrown hair which could be

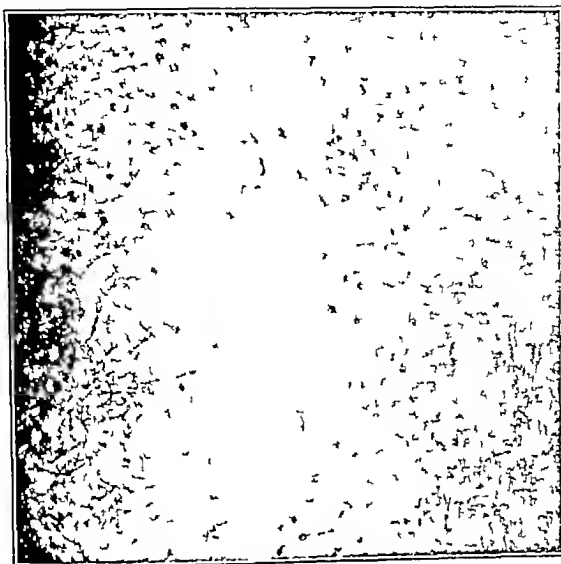


FIGURE 2 Lateral View of the Thigh after Five and a Half Months of Vitamin C Free Diet

Note the hyperkeratotic papules surrounding the hair follicles

After one hundred and thirty-four days had elapsed small perifollicular hyperkeratotic papules began to develop over the buttocks and the posterior aspects of the calves (Figs. 2 and 3). There was noticeable fragmenta-

tion of the hyperkeratotic plug was picked or scraped off leaving a small slightly bleeding crater. Associated with these papules was a marked dryness of the skin, particularly over the extensor surfaces, and the backs

#### ADDITIONAL DATA (continued)

Differential White-Cell Count (per cent) (76) 70 P 26 L 2 M 1 E 1 B (132) 55 P 36 L 4 M 1 E 1 B (180) 60 P 24 L 13 M 2 E 1 B  $\pm$  (704) 66 P 23 L 8 M 2 E 1 B  
Hematocrit (0) 0.48 (77) 0.50 (87) 0.49 (107) 0.45 (122) 0.45 (122) 0.47 (154) 0.48 (180) 0.46  $\pm$  (194) 0.39 (198) 0.38 (203) 0.36 (205) 0.41  
Sedimentation Rate (mm per minute) (28) 0.4 (75) 0.01 (93) 0.03 (111) 0.05 (145) 0.2 (178) 0.1 (191) 0.2.  
Blood Sodium (milliequival per liter) (33) 142 (43) 136 (78) 143 (89) 147 (122) 149 (146) 137 (187) 136  $\pm$  (198) 143  
Blood Complement normal titer throughout (78 121 152 190)  
Guthrie Test negative throughout (36 53 67 88 105 110 120 129 134 145 160 170 192)  
Bleeding Time (1/2 seconds) (71) 124 (102) 290 (122) 190 (149) 182 (178) 110 (187) 125  
Clotting Time (1/2 minutes) (71) 9 (102) 8 (122) 12 (149) 10 (187) 6  
Guaiac Test on Stool negative throughout (54 95 120 139 145 192)  
Urine (sugar albumin and sediment) normal throughout (0 55 120 130 188 192)  
Serum Proteins (gm per 100 cc) (93) 6.5 4 G as 4.3 2.2 (121) 5.0 (154) 6.5 (187) 7.1  
Chest X-Ray Film normal throughout (0 46 85 112 146 177)  
Electrocardiogram normal throughout (35 85 112 146 177)  
Red-Cell Fragility Test (156) normal

Determination at the Children's Hospital (Boston) Laboratory

(Numbers in parentheses refer to days of diet)

Vitamin C therapy started on the one hundred and thirty-second day of the diet.

of the hands became markedly roughened, the pores standing out in exaggerated fashion. The similarity between the lesions of vitamin A deficiency and those of vitamin C deficiency has been previously pointed out.<sup>20, 21</sup> In order to determine the presence or absence of vitamin A deficiency a biophotometric test<sup>22</sup> was done by Dr Harold J. Jeghers, of the Boston City Hospital. This showed perfectly normal visual adaptation in the dark. At the same time vitamin A determinations done on the plasma were within normal limits, both in our laboratory and that at the Children's Hospital. These findings, coupled with the fact that at least 30,000 international units of vitamin A had been taken daily,—the normal requirement being only 5000 units,<sup>22</sup>—seem to us to rule out vitamin A deficiency as a possible cause for these lesions.

After one hundred and sixty-one days of the diet, the

compared with a normal control<sup>18</sup>, histological study showed ample intercellular substance and capillary formation (Fig. 6). At the end of one hundred and eighty-two days, after the plasma ascorbic acid had been at zero for one hundred and forty-one days, the white-cell-platelet ascorbic acid at zero for sixty-one days, and the petechiae apparent over the lower limbs for twenty-one days, a similar wound was made in the left mid-back.\*

The skin sutures were removed on the sixth postoperative day, at which time the wound seemed to be progressing normally.

On the tenth postoperative day, under Pentothal anesthesia, a biopsy was made of the wound through an incision transverse to it and again extending down to the sacrospinalis muscle. Beneath the skin, which appeared well healed, there was no healing of the wound, which



FIGURE 3 Posterior View of the Thigh after Five and a Half Months of Vitamin C-Free Diet

*Note the fragmentation of the hairs*

plasma ascorbic acid having been zero for one hundred and twenty days, there appeared for the first time small perifollicular hemorrhages or petechiae over the lower legs (Fig. 4). These lesions did not fade on pressure and were not elevated. They seemed to occur in greatest numbers after the subject had been standing for some time (five hours), appearing for the first time, in fact, following a long period of operating. First seen over the inner and extensor aspects of the lower legs, the petechiae crept upward as the experiment progressed, until at the end of six months they were abundant over the lower thighs, where they seemed to take the place of the hyperkeratotic lesions already described.

Following the administration of vitamin C all skin lesions rapidly cleared (Fig. 5).

#### Wound Healing

At the end of three months, after the plasma ascorbic acid had been zero for forty-four days, a sizable wound was made in the right mid-back of the subject. Ten days later biopsy of this wound showed good healing, as

was filled with unorganized blood clot (Fig. 7). This was in marked contradistinction to the findings at three months, when there was perfect wound healing. So little healing had occurred that it was necessary to insert a small rubber drain, and the wound was brought together only with silk sutures through skin and subcutaneous tissue.

Sections of this wound, examined by Dr. Frederick Parker, Jr., of the Boston City Hospital, and Dr. S. Bar-

\*A 6-cm. transverse incision was made in the left mid-back under anesthesia (1 per cent novocain). The latissimus dorsi aponeurosis was divided in the plane of its fibers and the anterior sacrospinalis muscle, 1 to 2 gm. of which was removed. The sacrospinalis fascia was then closed with interrupted sutures of plain No. 00 catgut. Considerable difficulty was experienced in approximating the edges of this fascia; the sutures tearing out with pressure. (No such difficulty had been encountered at the previous operation.) The latissimus dorsi aponeurosis was then approximated with a running suture of plain No. 00 catgut and silk to the skin.

Postoperatively the movements of the subject were unrestricted as at the previous operation, but on the second postoperative day there was elevation of temperature to 101°F. On examination at this time the wound appeared perfectly normal and it was left alone. The subject being admitted to the hospital for forty-eight hours. Thereafter he again continued his movements unrestricted as before.

Wolbach of the Harvard Medical School, showed lack of intercellular substance and capillary formation (Fig. 8) as had been found by Wolbach<sup>3</sup> in the wounds of scorbutic guinea pigs. This finding was in marked contrast to the section from the wound biopsy at the end of three months (Fig. 6).

Immediately after the biopsy the subject began daily to receive 1000 mg. of ascorbic acid intravenously continuing as before on the same vitamin C-free diet (see below.) After forty-eight hours the activities were again unrestricted, the drain being removed at this time. On the tenth postoperative day another biopsy specimen was taken from this wound. There was good healing, the sections showing ample intercellular substance and capillary formation as seen in Figures 9 and 10.

which over the entire period of vitamin C deficiency amounted to slightly over 6000 cc., no anemia developed. The hemoglobin showed a slight fall during the third month of the diet, but rose to normal after the intake of 0.5 gm. of ferrous sulfate daily (Fig. 1). During the week of intravenous vitamin C therapy the hemoglobin dropped sharply to 79 per cent as a result of a blood loss of about 120 cc. daily for plasma and white-cell-platelet determinations over a five-day period. This level was maintained for another week in spite of cessation of blood loss and although there was a good reticulocyte response. With a normal diet, which included large amounts of orange juice daily the hemoglobin thereafter rose rapidly reaching 101 per cent after another ten days.



FIGURE 4 Anterior View of the Lower Legs after Six Months of Vitamin C Free Diet

Note the petechiae

#### Teeth and Gums

During the first five months of the diet no changes were grossly apparent in the teeth or gums. A competent dentist pronounced the gums to be normal in appearance at the end of this time.

At the end of six months when clinical scurvy as manifested by the perifollicular hemorrhages over the legs, had been present for three weeks, examination of the gums and the teeth was made by Drs. A. P. Young and P. E. Boyle, of the Harvard Dental School. They found that the gums were slightly more boggy on pressure than usual but no other gross changes could be seen. A biopsy specimen of the gingiva at this time was absolutely normal. Of interest is the fact that although the gross findings were negative, x-ray films of the teeth taken at this time showed occasional interruptions of the lamina dura.

#### Anemia

During the period of vitamin C deficiency there were four episodes of acute blood loss by venesection (Fig. 1). There was, moreover, mild chronic loss of blood as a result of various blood determinations. In spite of this loss,

#### Leukopenia

At the onset of the experiment the white-cell count averaged around 5000 and no appreciable variation from this figure occurred until after one hundred and thirty two days of the diet (Fig. 1). At this time the count fell to 3500, the differential count being normal. Except for slight rises following an episode of acute blood loss and after the last experimental wound the white-cell count fluctuated between 3200 and 5000 during the rest of the experiment remaining for the most part at the lower level. Following the administration of vitamin C there was a rise in the white-cell count to 5000 and later to 9000.

#### Infection

There was almost complete freedom from respiratory infection throughout the experimental period covering the months of October to May. Only two very transient and mild attacks of coryza were noted, each lasting but a few days. In previous winters it has been not uncommon for the subject to suffer from frequent, severe upper respiratory infections. Throughout the period of deficiency

<sup>1</sup>Hemoglobin determinations and other blood studies were done from the courtesy of Dr. F. I. Lerner of the Bernard Memorial Laboratory at the City Hospital.

there developed an occasional furuncle over the back of the neck, but each cleared up in normal time.

Blood-complement determinations\* were done at the end of the third, fourth, fifth and sixth months of the diet, the last after clinical scurvy had been apparent for three weeks (Fig 1). Each determination showed a perfectly normal titer as compared with a control.

#### *Weight Loss*

There was a gradual and continual weight loss for the first five and a half months of the experimental period reaching a maximum of 27 pounds at the end of this time. This drop in weight can be criticized as adding an additional unknown factor to the experiment. We believe it difficult, however, for anyone to remain on a diet absolutely free of vitamin C over a long period

about the mechanisms involved, the subject performed two grades of work on a motor-driven treadmill (walking and running). After ten days, during which the subject received vitamin C intravenously but remained on the deficient diet, the experiment was repeated. A control test was made seven weeks after the normal diet had been resumed. The data of Robinson<sup>23</sup> covering the same age group were used for comparison.

During a period of moderate work,—a walk for four and a half minutes on a grade of 8.6 per cent at a rate of 3.5 miles per hour,—both before and ten days after the beginning of vitamin C therapy, the subject's heart rate was nearly maximal, being about 40 beats per minute higher than on any of the men studied by Robinson. In the control test seven weeks later the heart rate after the same work was within normal limits. Throughout

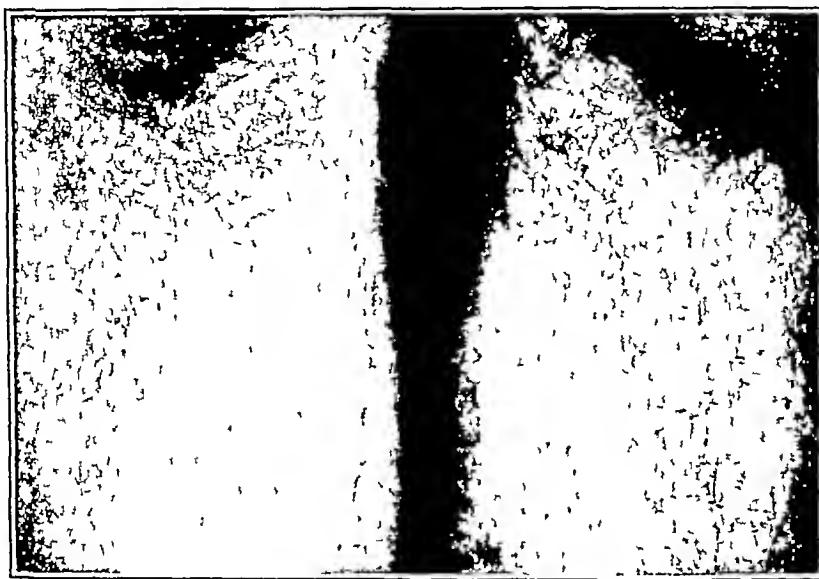


FIGURE 5 *Anterior View of the Lower Legs after a Week of Intravenous Vitamin C Therapy*

*Note the fading of the petechiae as compared with those in Figure 4*

without losing weight, since in order to avoid traces of the vitamin the diet must be restricted essentially to eggs, cheese, bread, butter and sucrose.

#### *Fatigue*

From the beginning of the third month of the diet there developed a feeling of fatigue which became progressively more marked. Measurement of this weakness was at first attempted by an ergograph. The number of contractions at the rate of one per second, made by the right hand against a standard resistance showed only a slight drop during the period of vitamin C deficiency, falling from 59 at the outset to 42 at the end of the experiment. A week after institution of the ascorbic acid therapy, while the subject was still on the diet, the number of contractions increased slightly to 49, a rise which can hardly be considered significant.

At the end of the six months a fatigue test was carried out of the Fatigue Laboratory of Harvard University (Table 1). In order to determine the extent to which the capacity for work was reduced and to learn something

this moderate work the oxygen consumption was within normal limits in each experiment.

During a harder grade of work,—a run at a rate of 7 miles an hour to exhaustion,—the subject's performances while in the scorbutic state and directly after the vitamin C therapy showed considerable differences. In the state of complete vitamin C deficiency he was able to run for only 16 seconds, whereas following ascorbic acid therapy he ran for 66 seconds, in spite of the fact that at this second experiment the hemoglobin was 13 per cent lower and the oxygen capacity was 7.6 millimol per liter as compared with 8.0 millimol in the first test. In the control experiment after the normal diet had been resumed the subject ran for 84 seconds. This performance was still inferior to the 270 second average of other men of this age. Both before and after vitamin C therapy the maximal heart rates were about the same, reaching 190 beats per minute, and in both experiments during this maximal work the minute-oxygen consumption per kilogram of body weight was but three fourths the average found by Robinson. These were normal in the control experiment performed seven weeks later. This indicates an incapacity for aerobic work unrelated to vitamin C deficiency.

\*Blood-complement determinations were done through the courtesy of Dr. C. P. Emerson of the Thorndike Memorial Laboratory, Boston City Hospital.

but does not diminish the significance of the better performance following vitamin C therapy. Despite his inability to reach a normal level of oxygen consumption while on the diet, the subject's capacity for anaerobic work, as measured by a hand ergograph, was undiminished even while in the scorbutic state (Table 1).

The subject accumulated a lactate concentration of 82 mg. per 100 cc. before and 104 mg. after the administration of vitamin C. The oxygen debts were 3.29 and

TABLE 1 *Fatigue Tests*

D	April 26 (Scorbutic State)	May 6 (After Vitamin C Therapy)	June 26 (Control)	Nov. 11 Range
Duration of work (mi.)				
Moderate work	4.5	4.5	4.5	15
Maximal work	0.2	1.1	1.4	3-5
Ergograph (lb.)	52.0	49.0		40-70
Oxygen consumption (cc/kg./min.)				
Moderate work	29.9	27.2	27.3	25-30
Maximal work	37.8	36.7	40.3	40-60
Oxygen debt (liters)	3.29	4.9"	5.55	
Heart rate (beats/min.)				
Moderate work	182	178	140	150-180
Maximal work	180	191	190	160-195
Recovery (1 min.)	161	180	140	140-160
Recovery (10 min.)	105	103	11	90-120
Recovery				
Oxygen consumption (liters)				
0-3 min.	2.58	8"	3.48	
3-15 min.	5.02	5.54	5.5	
Blood lactate (mg./100 cc.)				
5 min.	82.0	104.4	104.0	
10 min.	65.1	105.5	93.3	
15 min.	51.6	87.6	75.0	
30 min.	28.1	51.6	35.6	
45 min.	22.4	22.4	31.2	
60 min.	24.4	13.7		
Blood sugar (mg./100 cc.)				
5 min.	127	122	125	
10 min.	94	115	114	
15 min.	100	113	120	
30 min.	100	104	110	
45 min.	109	99	118	
60 min.	106	106		
Insulin-tolerance curve (sugar in mg./100 cc.)				
2 min.	88	100		
10 min.	83	90		
15 min.	76	80		
20 min.	74	72		
25 min.	66	65		
35 min.	67	70		
45 min.	69	83		
60 min.	74	100		

497 liters, respectively. These higher figures after the vitamin C therapy were associated with the increased performance in the run. This may have been the result in part of improved skill but it should be pointed out that the capacity for supplying oxygen was somewhat lowered in the second test.

The performance of the subject while in the scorbutic state placed him in the same category as the Group A of Robinson, consisting of men in the eighth decade of life for whom the five-minute walk was maximal work. The heart rate during recovery was higher than that observed by Robinson. Following treatment with ascorbic acid the rate fell more rapidly during recovery despite a slightly higher initial value, a higher blood lactate concentration and a greater oxygen debt.

Of considerable interest are the blood lactate levels

following the fatigue test performed when the subject was in a scorbutic state. There was a normal rate of disappearance of the blood lactate for the first fifteen minutes of the recovery period. During the following half hour the rate of disappearance was much decreased being about half the normal rate. After the vitamin C therapy the rate of disappearance of the blood lactate was normal throughout the recovery periods of the tests made while the subject was still on the diet and also following the control run seven weeks later.

Studies made on samples of arterial blood, drawn when the subject was in the basal state, before and after treat-

TABLE 2. *Arterial Blood Studies Before and After Vitamin C Therapy with the Subject in a Basal State*

D	April 26 (Scorbutic State)	May 6 (After Vitamin C Therapy)	Normal Range
Carbon dioxide content (ml./lit.)	21.5	21.5	20.0-23.0
Hemoglobin oxygen saturation (ml./100 g. Hb.)		10	8.0-9.5
Hemoglobin oxygen capacity (ml./100 g. Hb.)	8.34	60	8.52-9.44
Hemoglobin oxygen saturation (per cent)		91.5	93.0-99.0
Serum carbonic acid (mEq./liter)	2.0	3.10	4-5
Serum bicarbonate (mEq./liter)	25.3	23.8	24.0-27.0
Arterial carbon dioxide pressure (mm Hg.)	42.0	44.4	35-45.0
Plasma pH	7.40	7.34	7.35-7.45
Lactate (mEq./liter)	1.0		1.0-1.5
Sugar (mg./100 cc.)	111.0		90.0-110.0
Plasma chloride (mEq./liter)	107.1	106.4	103.0-107.0
Plasma protein (gm./liter)	62.0	65.2	63.0-68.0
Plasma inorganic phosphorus (mEq./liter)	2.4	1.7	1.6-3

ment showed no abnormalities except for a slight anemia (Table 2).

### Basal Metabolic Rate

Basal metabolic rates were frequently determined by the Benedict-Roth method beginning prior to the dietary period and continuing during the administration of parenteral vitamin C while the subject remained on the diet (Fig. 1). During the dietary period the metabolic rate fell as low as -22 per cent but after the administration of vitamin C was started while the subject was still on the diet, values as low as -18 per cent were obtained. At the Harvard Fatigue Laboratory where the metabolic rate was determined by the open-circuit gasometer method there was an increase from -6 to -3 per cent after the institution of vitamin C therapy. It is doubtful therefore, whether the fall in basal metabolic rate could in any way be attributed to vitamin C deficiency. It was probably due to weight loss or inanition or both. Basal metabolic rates were done daily after the parenteral ascorbic acid was started both before its administration and one and a half to two hours thereafter. It is interesting that during the first four days the basal metabolic rate uniformly fell after the administration of 1000 mg. of ascorbic acid intravenously (Table 3). During this time the subject was becoming saturated with the vitamin (see below). Following this period of saturation the basal metabolic rate two hours after the administration of ascorbic acid was consistently higher than it was before its injection.

### Capillary Fragility

During the entire experiment the capillary fragility test, as described by Gothlin,<sup>24, 25</sup> remained absolutely negative (Fig 1). At the end of five months, when the petechiae were beginning to appear over the legs, a pres-

a portion of sacrospinalis muscle was removed and subsequently analyzed for total soluble phosphorus and for phosphagen phosphorus content.\* The total phosphorus content was low, being only 111.5 mg per 100 gm. of muscle. The phosphagen phosphorus content was high,

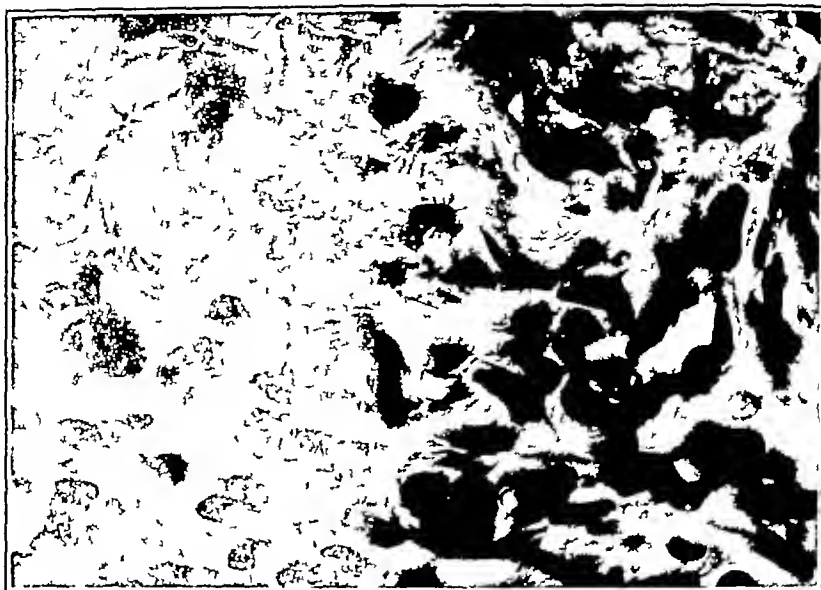


FIGURE 6 Biopsy Specimen Removed after Three Months of Vitamin C-Free Diet Eosin and methylene blue stain ( $\times 650$ )

Note the numerous capillaries and the abundance of intercellular substance in the granulation tissue

sure of 100 mm of mercury was applied to the arm for ten minutes by means of a blood pressure cuff. This brought out twenty-two petechiae in a measured area 6 cm in diameter. Among 8 controls, 7 showed more petechiae at the end of ten minutes than did the subject. Dr. C. J. Farmer, at Northwestern University, performed

TABLE 3 Effect of Intravenous Ascorbic Acid (1000 mg) on the Basal Metabolic Rate of the Scorbutic Subject

DATE	BASAL METABOLIC RATE	
	BEFORE THE INJECTION OF VITAMIN C %	1½ HR. AFTER THE INJECTION OF VITAMIN C %
April 28	0.0	-3.0
April 29	-15.4	-16.4
April 30	-7.5	-11.2
May 1	0.0	-18.7
May 2	-16.7	-9.0
May 3	-3.3	-3.3
May 4	-12.3	-8.3

a negative pressure (Dalldorf<sup>26</sup>) test on the arm of the subject after five months and two weeks of dieting. This also was perfectly normal, 450 mm (mercury) of negative pressure being required to produce any petechiae.

### Blood Pressure

The blood pressure remained at a constant level of 120 systolic, 70 diastolic, until immediately following the fourth episode of blood loss on the one hundred and fifty-fifth day of the diet, when it fell to 90/60. During the next week the systolic pressure rose to 98, but it never exceeded this level until the ascorbic acid was started, when it promptly rose.

### Muscle Phosphorus and Phosphagen

At the time of biopsy of the second experimental wound

being 50.4 mg per 100 gm. of muscle, or 45 per cent of the total phosphorus content. In normal muscle the phosphagen is only about 35 per cent of the total soluble phosphorus.

After a ten day period, during which the subject remained on the same vitamin C-free diet but daily received 1000 mg of ascorbic acid intravenously, another piece of muscle was analyzed, this time from the thigh. The total soluble phosphorus was considerably increased, being 145.9 mg per 100 gm, while the phosphagen phosphorus was only 45.6 mg per 100 gm, or 31 per cent of the total muscle phosphorus.

### Miscellaneous

Two insulin tolerance tests were done (Table 1).† Each was obtained following the intravenous injection of 31 units of insulin. The tests were made under identical conditions, and while the subject was in the basal state. It is apparent that vitamin C had no influence on insulin tolerance. Glucose tolerance tests were also normal.

A gastric analysis done after five months of the diet showed only 1 unit of free acid and only 3 units of total acid, and after histamine 22 units of free acid and 27 units of total acid. After eleven days of intravenous administration of ascorbic acid, while the subject was still on the diet, analysis of the gastric contents again showed only 1 unit of free acid and 3 units of total acid, but this time, after the administration of histamine, there were 33 units of free and 42 units of total acid.

\*Muscle phosphorus and muscle phosphagen phosphorus determinations were done through the courtesy of Dr. Steven Horvath of the Harvard Fatigue Laboratory.

†Insulin tolerance tests were done through the courtesy of Dr. John W. Thompson of the Harvard Fatigue Laboratory.

Other determinations which included serum protein, lipids, sedimentation rates, hematocrits, bleeding and clotting times, examination of stools and urines for blood (with complete analysis of the latter), chest x-ray films and electrocardiograms were within normal limits (Fig. 1). There was a slight fall of the blood sodium level from 142 to 136 milliequivalents per liter just before the ascorbic acid was begun. Following six days of ascorbic acid therapy the blood sodium regained the normal level.

An electroencephalogram made between the fourth and fifth months of the diet was negative.\*

#### *Saturation of Vitamin C*

Following the first biopsy of the second experimental wound, saturation with vitamin C was begun the same

levels were higher, the latter being 3, 16 and 28 mg per 100 cc. respectively on the first three days of the saturation regime. This almost normal white-cell platelet value on the third day together with the very gradual drop in the plasma level of the vitamin on that day may be taken as indication that saturation of the blood occurred some where between the third and fourth days.

Examination of the urinary output of the vitamin immediately reveals that the amount, as determined by the Evelyn-Malloy<sup>1</sup> method is much smaller than has been obtained by the Harris titration method, if the subject may be considered saturated after the fourth day. In determining the values in the urine, great care was taken in our laboratory to avoid any ceiling in the method by multiple dilutions of the urine samples.

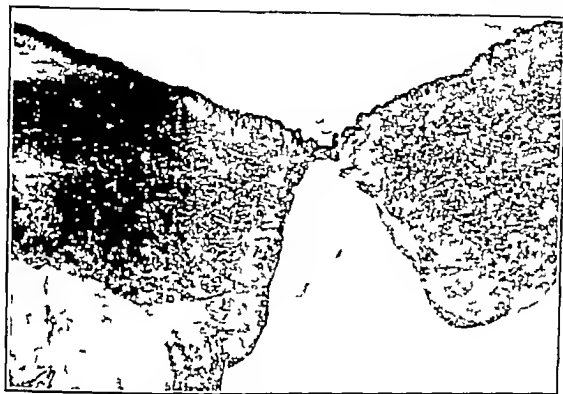


FIGURE 7 Biopsy Specimen Removed after Six Months of Vitamin C-Free Diet. Eosin and methylene blue stain ( $\times 15$ )

*This section shows complete lack of healing. The large space was occupied by an unorganized blood clot.*

vitamin C-free diet being continued. For this purpose 1000-mg doses of ascorbic acid were given daily after the manner of Wright, Lilienfeld and MacLennan.<sup>27</sup> It was believed that the intravenous route was the best method of saturation, since oral doses may introduce unknown and perhaps variable absorption factors<sup>28-30</sup> as well as a time factor in the ensuing saturation curves. After preliminary plasma and white-cell platelet determinations the vitamin was injected, following which hourly plasma and urine determinations were done. The plasma and urine determinations are represented in Figure 11.

Early in the experiment it had been found that even with a plasma of zero and no intake of the vitamin the titration method of Harris<sup>11</sup> gave considerable values in the urine, undoubtedly owing to the presence of reducing substances other than vitamin C.<sup>31</sup> For this reason the recently described method of Evelyn Malloy and Rosen<sup>1</sup> was used.

It can be seen on examination of Figures 11 and 12 that on the first day the plasma C content fell very rapidly during the first three hours after injection of the vitamin, reaching zero at the end of five hours. On each succeeding day the initial plasma and also the white-cell platelet

It becomes evident on examination of Figure 11 that there is an apparent renal threshold, as described by Faulkner and Taylor using the Harris titration. According to our findings, however, this threshold does not occur at a plasma value of 14 mg per 100 cc., as described by them and others, but rather with a plasma value of about 0.85 mg in the normal adult, as shown by the April 30 figures. Moreover the plasma saturation and urinary excretion curves suggest that in the totally vitamin C-deficient state this renal threshold may be lower and that as saturation with vitamin C takes place it rises to normal (April 27 to 30 figures). On the other hand the appearance of ascorbic acid in the urine coincidental with low plasma levels (in the first three curves) may be due to a lag phenomenon.

Examining the curves again it may be noted that during the process of saturation with vitamin C the output of the vitamin in the urine was on two occasions greater during the second hour than during the first hour (April 30 and May 2). On these two days the volume of urine excreted was considerably greater during the second hour than during the first hour. On the other days during the saturation period the volume was greater in the first than in the second hour and it will be noted that the excretion of the vitamin was also always greatest during

\*Electroencephalography was performed through the courtesy of Dr. F. A. Gibbs, of the Boston City Hospital.



the first hour. This would suggest that while the organism is in a vitamin C-deficient state the output of ascorbic acid may depend not only on its plasma level and on the renal threshold but also on the amount of urine excreted. Of interest in this respect is the finding of Sendroy and Miller<sup>33</sup> that renal function is a factor in the excretion of ascorbic acid, and that of Wright and MacLennan<sup>34</sup> that vitamin C may be excreted slowly in cases of kidney damage. Following saturation of the subject, however, the excretion of vitamin C was always greatest during the first hour after the injection, no matter how the urinary output was made to vary.

#### *Effect of Vitamin C Therapy*

Within twenty-four hours after the administration of the vitamin a subjective improvement was noted, there being

measured by the fatigue test, and, of course, the wound healing, there were no noteworthy changes during the vitamin C therapy while the subject remained on the diet. There was no gain in weight during this time.

#### COMMENT

##### *Wound Healing*

Since the emphasis by Wolbach and Howe that the fundamental lesion of scurvy is a deficiency of intercellular substance and capillary formation, there has been increased interest in the surgical significance of the vitamin. The experimental work of Lanman and Ingalls<sup>4</sup> and of Taffel and Harvey,<sup>35</sup> showing that the wounds of scorbutic



FIGURE 8 *Biopsy Specimen Removed after Six Months of Vitamin C-Free Diet. Eosin and methylene blue stain ( $\times 350$ )*

*Note the newly formed fibroblasts having no intercellular substance between them. Old collagen may be seen at the bottom and extending down and to the right from the upper left hand corner.*

a marked alleviation of weakness and languor. This improvement seemed to progress during the next four or five days. It is possible, of course, that considerable or even all the effect was due to suggestion.

The skin changes were remarkable. At the end of six days the petechiae had faded considerably, and the skin had returned from a rough to a smooth state, although hyperkeratotic papules were still present. Between twelve and fourteen days after the institution of the vitamin C therapy the petechiae had entirely disappeared, but traces of the papules remained over the buttocks for three weeks.

Although the hemoglobin fell following the commencement of vitamin C therapy, it is of interest that the blood pressure, which had been somewhat below the subject's normal since the last episode of acute blood loss, almost immediately began to rise after the vitamin C had been given.

On the third day after the vitamin was begun a slight blurring of vision was noticed when the eyes were focused on distant objects. This cleared up in twenty-four hours, and may have been due to diffusion of ascorbic acid into the lens.

Except for the increased ability to do aerobic work, as

guinea pigs healed slowly and with poor tensile strength, received support from the clinical work of certain investigators,<sup>36-39</sup> notably Wolfer, and Archer and Graham. The clinical evidence for the necessity of the vitamin for wound healing lay somewhat open to question, however, since the cases reported were of necessity, poorly controlled with respect to other variable factors important in wound healing, notably other avitaminoses, infection, surgical technic and so forth. Although it is to be remembered that only one case is considered here, all such variables were excluded, and the lack of wound healing must be attributed to ascorbic acid deficiency alone. The mere fact that the biopsy sections showed striking resemblance to those from the wounds of scorbutic guinea pigs would appear as conclusive evidence that the lack of healing was due not to infection, in

creased tension or other such factors but to vitamin C deficiency

### *Significance of Plasma Vitamin C Levels*

It should be kept in mind that normal wound healing occurred after three months of vitamin C deficiency, when the plasma ascorbic acid had been zero for as long as forty four days<sup>15</sup>. This, together with the other negative findings at that time, suggests that the plasma ascorbic acid is a poor index of the vitamin C status of the patient.

Lack of controlled cases may possibly be responsible for the general belief that the plasma levels

suggests that multiple avitaminosis may bring on clinical vitamin C deficiency more rapidly. And it is to be remembered of course, that clinical vitamin C deficiency is practically always associated with some deficiency of vitamin B and perhaps also of the other vitamins. There is a known increased disappearance of vitamin C from both plasma and white cells in cases with infection,<sup>41-48</sup> and when growth or hyperthyroidism is a factor.<sup>49-50</sup> It is possible, moreover, that extreme muscular exertion may deplete the body of the vitamin more rapidly, and that scurvy would have appeared in the experimental subject much soon

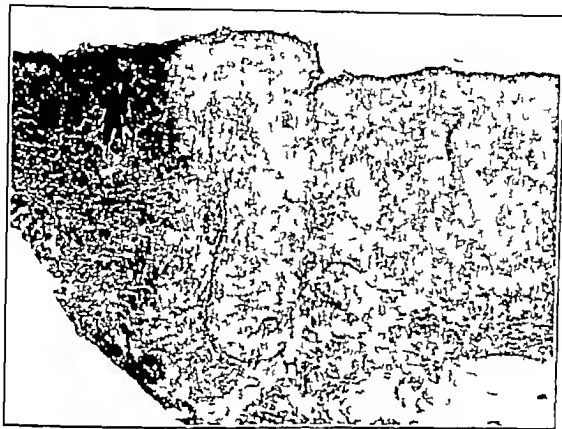


FIGURE 9 Biopsy Specimen Removed after Ten Days of Intravenous Vitamin C Therapy. Eosin and methylene blue stain ( $\times 15$ )

*This section shows complete healing of both the original wound and that of the biopsy, ten days later*

of the vitamin are a fair index of deficiency and that levels below 0.5 mg per 100 cc. are dangerously low.<sup>35-40</sup> As pointed out by Butler and Cushman<sup>19</sup> it would seem that the white-cell platelet level of the vitamin in the centrifuged blood is a much more accurate measure of deficiency. In this case the level reached zero just ten days before the hyperkeratotic papules appeared and thirty days before the appearance of the petechiae, at which time the plasma had been zero for one hundred and twenty days.

Why did so much time elapse before clinical scurvy appeared in this subject? The answer to this question must lie in the fact that there were no complicating factors such as growth infection or multiple avitaminosis. That Stark<sup>11</sup> showed signs of scurvy within ten weeks on a diet almost totally deficient in all the vitamins

er had he been constantly subjected to extreme muscular fatigue

### *Human Requirement*

Much has been written on the vitamin C requirement of human adults, and many methods<sup>17-21, 51-56</sup> have been evolved and employed for its estimation. The majority are necessarily based on the assumption that saturation is the optimal state for the individual, a postulate having little evidence for its support. Estimations of the daily requirement have varied between 20 and 100 mg per 100 cc., the majority of workers setting 30 mg. as the daily minimum.<sup>51</sup>

It is unfortunate that in this experiment the point at which the subject became saturated cannot be accurately determined. Although the blood level of the vitamin had returned to normal by

the fourth day of the saturation period, the urinary output was not maximal by the sixth day. Taking into consideration the total amount lost in the urine (about 1 gm) 4 to 6 gm may be considered as roughly the maximal amount of ascorbic acid necessary to resaturate this individual. Since the first signs of scurvy appeared after one hundred and thirty-two days of total vitamin C deficiency, the maximal daily utilization of the vitamin must have been between 30 and 45 mg. It is possible that the true requirement lies somewhat below this figure. On the other hand, this esti-

raises the question, however, as to whether those commonly described<sup>57</sup> as typical of scurvy may not be at least in part due to pre-existing or superimposed gingivitis or dental caries or both. Supporting this hypothesis is the fact that in edentulous scorbutic patients no gingival changes are commonly seen. Of interest are the x-ray films of the teeth taken during the scorbutic state, particularly since they are consistent with the alveolar lesions found by Boyle in scorbutic guinea pigs<sup>58-60</sup>. In these films slight but definite interruptions of the lamina dura can be made out, which presuma-

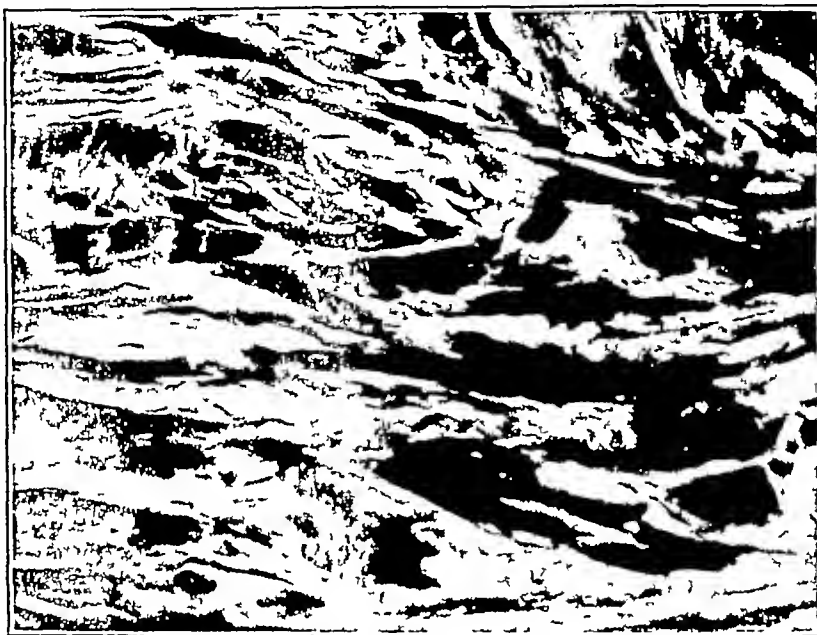


FIGURE 10 Biopsy Specimen Removed after Ten Days of Intravenous Vitamin C Therapy Eosin and methylene blue stain ( $\times 600$ )

*Note the abundant, newly formed fibroblasts, with collagen between them*

mate would of course be elevated if infection, multiple avitaminoses, hyperthyroidism and possibly increased exertion had been factors in the experiment.

### *Teeth and Gums*

Grossly the teeth and gums showed no marked changes during the entire dietary period, although very slight bogginess was found one week before the institution of vitamin C therapy. On brushing the teeth there was no trace of bleeding at any time. Immediately after the fatigue test, while in the scorbutic state, however, the subject did show for the first and only time a small hemorrhage at one gingival margin, a finding which suggests that had he been exposed to such fatigue throughout the experiment, signs of scurvy might have appeared much earlier. The lack of changes in the gums and teeth during the entire period

bly result from atrophy of alveolar bone and its replacement with collagen-free fibrous tissue. Slight but definitely noticeable changes toward the normal could be discerned in the roentgenograms taken five weeks after the subject had resumed a normal diet. It is possible that x-ray films showing such interruptions of the lamina dura may be one of the best criteria for the diagnosis of incipient scurvy.

### *Anemia*

The fact that no appreciable anemia occurred in the subject until the administration of ascorbic acid was begun, in spite of a blood loss of over 6000 cc during the six-month period, is not in accord with the conclusions of Mettier, Minot and Townsend<sup>61</sup> and of Parsons and Hawksley<sup>62</sup>—which have already been challenged by several workers, notably Cooley<sup>63</sup> and Gingold<sup>64</sup>—to the

effect that vitamin C deficiency per se may cause diminished hematopoiesis

### Resistance and Infection

There is at present a widespread belief that vitamin C deficiency is an important cause of lowered resistance to infection. This is based in part on the well known fact that there is much more rapid disappearance of the vitamin from

### Leukopenia

During the dietary period there was a slight fall in the white-cell count, but since the normal count for the subject was apparently only 5000 this cannot be considered as significant. The rise to 9000 occurring after the beginning of vitamin C therapy is consistent with the findings of other workers,<sup>13</sup> who have noted moderate leukocytosis

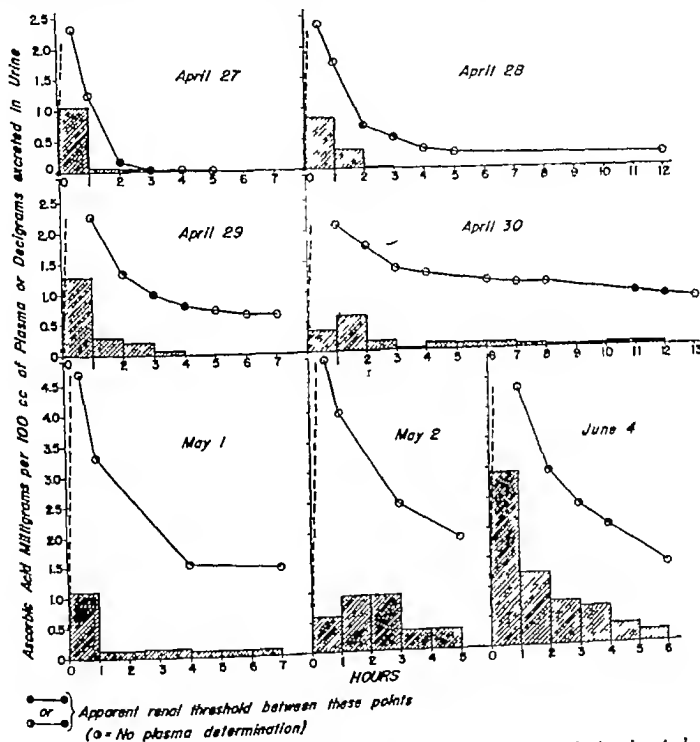


FIGURE 11 Plasma and Urine Vitamin C Levels Following Saturation with Ascorbic Acid

both plasma and tissues in cases of infection and in part on results in experimental animals.<sup>48-49</sup> Moreover Ecker<sup>70-71</sup> and others<sup>7</sup> have recently reported lowered titers of blood complement in scurvy. Although the literature supporting the value of vitamin C in sepsis is extensive, the complete lack of infection in this experimental subject over the period of deficiency raises doubt as to whether vitamin C per se is a marked factor in lowering the resistance of an adult. Moreover, blood-complement titers showed no fall whatsoever even after the appearance of frank scurvy

following the intravenous administrations of ascorbic acid in cases of leukopenia

### Fatigue

The belief that scurvy is characterized by languor and incapacity for work is well borne out by this experiment. Subjectively, weakness was first noticed at about the end of the third month becoming progressive as time went on. Although no marked change could be found in the muscular activity of the forearm as measured by an ergograph both for a single contraction and for

contractions each second to exhaustion, the results when the subject ran on a treadmill were striking. Although a considerable part of his inability to run over 16 seconds must be attributed to factors other than vitamin C deficiency, he was able to run 66 seconds following the parenteral administration of ascorbic acid while on the same diet, even though the hemoglobin was 13 per cent lower. Of interest, also, is the fact that the heart rate fell more rapidly during the recovery period following the administration of the vitamin. Moreover, it will be noted that the blood lactate curve was definitely abnormal in the scorbutic

this would seem to throw serious doubt on the contention that such tests are a good index of subclinical vitamin C deficiency,<sup>74</sup> in spite of the fact that frequently in cases of scurvy such tests are positive, and that in many such cases vitamin C therapy rapidly clears up all signs of such abnormal fragility. Lack of correlation between capillary fragility and vitamin C deficiency is also being found by other workers,<sup>75</sup> and notably Farmer<sup>76</sup>

### Blood Pressure

Of possible significance was the fall in blood pressure which occurred and persisted after the last episode of acute blood loss (one hundred and fifty-fifth day), since it returned to normal after the administration of vitamin C, in spite of continuation of the vitamin C-free diet and blood loss. Pertinent in this respect are the facts that in animals relatively large amounts of vitamin C are stored in the adrenal glands, and that scorbutic guinea pigs have diminished adrenocortical hormone<sup>77</sup> and at autopsy show atrophy of the adrenal cortex.<sup>78</sup> Toward the end of the experiment, almost coincidentally with the fall in blood pressure, the blood sodium fell to 136 milliequiv per liter, rising to 142 milliequiv directly after vitamin C therapy. Whatever the cause of this lowered systolic pressure, it was not due to diminished blood volume, for this was normal at the end of the six-month period, as measured by the Gibson method.

### Glucose and Insulin Tolerance

There are at present many conflicting views as to the effect, if any, of vitamin C on carbohydrate metabolism. It has been reported that there is a lowered glucose tolerance in scorbutic guinea pigs<sup>79</sup> and that the administration of vitamin C results in increased sensitivity to insulin both in normal subjects and in diabetic patients.<sup>80-84</sup> In contrast to these findings are the entirely negative results of other workers<sup>85-87</sup> who have been unable to show any relation between vitamin C and carbohydrate metabolism. In agreement with the latter conclusions are the insulin-tolerance and glucose-tolerance curves of the experimental subject, which were within normal limits while he was in the scorbutic state.

### Basal Metabolic Rate

Because vitamin C has relatively strong reducing properties, there is a widespread belief that it serves primarily as a "hydrogen transport agent."<sup>88</sup> Here again the experimental findings are in conflict, some investigators<sup>89, 90</sup> reporting a decrease in metabolic rate in scorbutic guinea pigs, others<sup>91</sup> an increase.

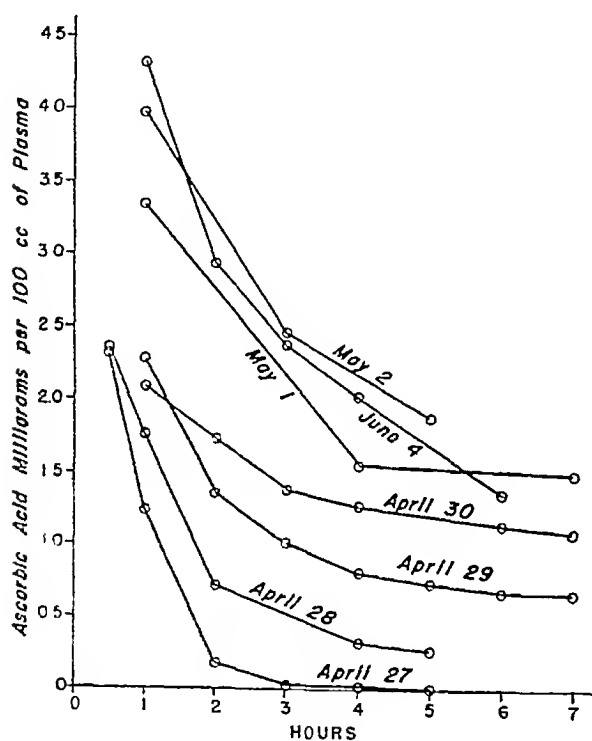


FIGURE 12 Plasma Vitamin C Saturation Curves

state. No hint as to the underlying physiologic mechanisms responsible for these differences before and after therapy could be gleaned from the laboratory determinations made coincidentally with these fatigue tests.

### Capillary Fragility

It should not be concluded that capillary fragility is not part of the underlying pathology of scurvy merely because the Gothlin and Dalldorf tests were negative throughout the experiment. The appearance of the petechiae in the lower extremities after a long period of standing suggests that hydrostatic pressure and capillary fragility were factors in their etiology. The experimental results suggest, however, that neither the Gothlin nor the Dalldorf test is a good measure of capillary fragility in early scurvy. Certainly

Since the basal metabolic rate of the experimental subject dropped to almost as low a level following the beginning of vitamin C therapy as during the period of deficiency, the variations during this period cannot be considered significant. These findings are in accord with the results of other workers.<sup>22</sup> Of interest, however, is the fact that during the saturation of the subject with vitamin C, the basal metabolic rate fell slightly directly after each injection of the vitamin, whereas after saturation had been completed no such fall occurred. Although this fall was constant during the saturation period it was generally very slight and its significance may therefore be open to question. A significant drop in metabolic rate following the administration of parenteral ascorbic acid to a scorbutic individual would, of course, suggest that by the introduction of the vitamin the individual's efficiency for utilization of oxygen was increased.

### *Metabolism of Vitamin C*

What part does vitamin C play in the physiology of the human organism other than as a prerequisite for the formation of intercellular substance? This question must at present remain unanswered. The abnormal blood lactate curves during the recovery period of the scorbutic subject after the fatigue test, the variations of the metabolic rate and the abnormal phosphorus and phosphogen contents of the striated muscle, all may serve as leads for future investigations into the metabolism of vitamin C.

### SUMMARY AND CONCLUSIONS

A normal active adult placed himself on a vitamin C-free diet supplemented by the other known vitamins for a period of six months. The findings in this state of pure vitamin C deficiency, that is, in the absence of factors such as multiple avitaminoses, infection, growth or other stress, were as follows:

One hundred and thirty-two days of a diet totally deficient in vitamin C were required for the first abnormal clinical signs—hyperkeratotic papules—to appear. 161 days were necessary for the appearance of the perifollicular hemorrhages of scurvy.

The plasma ascorbic acid level was zero for thirteen weeks before the first evidence of clinical scurvy was manifest. It is not necessarily, therefore, a good index of the vitamin C status of the individual.

The vitamin level in the white-cell-platelet layer of the centrifuged blood was a good index of the vitamin C status of the subject. This

level fell to zero shortly before the appearance of clinical scurvy.

Adequate wound healing occurred after the plasma ascorbic acid had been zero for forty-four days and when the white-cell-platelet ascorbic acid level was 4 mg. per 100 cc.

With total vitamin C deficiency failure of wound healing occurred. The tissues under these circumstances showed microscopically a lack of intercellular substance. Parenteral vitamin C alone brought about good healing and considerable intercellular substance appeared within ten days.

Hyperkeratotic papules containing ingrown hairs appeared over the buttocks and posterior aspects of the legs as a result of vitamin C deficiency; indeed they may be the first sign of such a deficiency.

There were no gross changes in the gums or teeth (with good pre-existing oral hygiene). Although the mouth was grossly negative x-ray films of the teeth showed interruptions of the lamina dura in early acute scurvy. Such an x-ray picture may be one of the better diagnostic criteria in early scurvy.

Vitamin C deficiency did not produce anemia.

After prolonged vitamin C deficiency there was inability to perform aerobic work, although the capacity for anaerobic work was undiminished. After a period of aerobic work in the scorbutic state the rate of disappearance of the blood lactate was abnormally slow.

During a six month period of total deficiency and after a month of clinical scurvy the blood complement titer was still normal. Over this period there was no evidence of lowered resistance to infection.

The Göthlin, Dalldorf and Rumpel-Leeds tests were negative, even in the presence of frank scurvy. These tests must therefore be poor indices of subclinical scurvy, even though they may in some cases produce petechiae which are cleared up by ascorbic acid therapy.

With severe vitamin C deficiency there was a fall in the blood pressure.

There was a lowering of the total phosphorus content of striated muscle, with an increase in the phosphagen phosphorus.

All the signs and symptoms of scurvy rapidly disappeared following the intravenous injection of ascorbic acid.

When the state of deficiency was complete the plasma ascorbic acid level fell to zero in five hours after injection of 1 gm. of the vitamin.

Although the blood became completely saturated (as measured by plasma saturation curves and white-cell-platelet levels) after 3 or 4 gm.

of ascorbic acid had been given intravenously, the tissues were not completely saturated at this time, since the urinary output of ascorbic acid was still well below maximal over a six-hour period

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## ALPHA AND BETA NEUTRAL KETOSTEROIDS (ANDROGENS)\*

Preliminary Observations on Their Normal Urinary Excretion and the Clinical Usefulness of their Assay in Differential Diagnosis

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THIS paper reports preliminary data on the twenty-four-hour urinary excretion of alpha, beta and total neutral ketosteroids|| by normal individuals of both sexes and of varying ages and by patients showing male sexual precocity or virilism.

The available evidence<sup>1-7</sup> indicates that the neutral ketosteroids (17 ketosteroids) arise from substances produced by the adrenal glands and male gonads. The total output is therefore considered to be a rough index of the combined activity of these two glands. The isolation of individual ketosteroids by Callow et al.,<sup>3-5</sup> Butler and Marrian,<sup>10</sup> Hirschmann<sup>11</sup> and Dorfman, Cook and Hamilton<sup>12</sup> affords evidence that whereas the alpha neutral ketosteroids probably arise from adrenal and gonadal secretions, the beta neutral ketosteroids are an excretion product only of the cells of the adrenal cortex.

Accepting this evidence as a working hypothesis, the rate of beta neutral ketosteroid excretion by the subjects mentioned above has been determined by a relatively simple but directly quantitative

colorimetric method reported elsewhere.<sup>14</sup> The data obtained not only augment the evidence favoring the adrenal cortex as the source of beta ketosteroids but also provide specific diagnostic criteria for the differentiation of adrenocortical hyperplasia, Cushing's syndrome without adrenal tumor and adrenocortical carcinoma.

### RESULTS

The data obtained on normal subjects (Table 1) show the following:

The average daily excretion of total neutral ketosteroids of children under seven years of age was very low (13 mg). It increased with age reaching an average of 40 mg between seven and twelve years and 8.2 mg between twelve and fifteen years. Adult men tended to excrete more ketosteroids (150 mg) than did adult women (10.2 mg). The level of total excretion of pregnant women (15.1 mg) approximated that of adult men.

The average daily alpha neutral ketosteroid excretion paralleled the total output. The aver-

\*This work was supported by the Department of Pediatrics, Harvard Medical School, and the Children's Hospital, Boston. This study was supported in part by grant from the Commonwealth Fund, New York City.

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||The terms "alpha" and "beta" refer to the spatial position of the hydroxyl group. The chemical separation of alpha and beta neutral ketosteroids is discussed here depends on the fact that beta ketosteroids (which include dehydroepiandrosterone and isandrosterone) may be precipitated with digoxigenin, leaving the other (alpha) ketosteroids (such as androsterone and etiocholan-3-[ $\alpha$ ]-17-one) in solution. The difference in the ketosteroid content of solution before and after precipitation, therefore, gives the beta ketosteroid content.

§§A comparison of the data obtained by this method due to Hirschmann should be given so the procedure employed for hydrolysis and extraction of the samples. The data reported here were obtained on individually employed four-hour specimens which were hydrolyzed by the commonly employed procedure of boiling for ten minutes with 150 cc. of hydrochloric acid per liter of urine followed by immediate extraction of the hormones with rapid benzene or carbon tetrachloride. Fractionation by solvent extraction in our laboratory indicates that the method of hydrolysis and some optimal. It results in some destruction of the method of estimation of the replacement of the beta hydroxyl group on which the estimation of the beta fraction depends. Consequently the results reported may include an underestimation of the total excretion and of the beta fraction as well as an overestimation of the alpha fraction. These errors will be considered in detail in a forthcoming paper.<sup>15</sup> They do not alter the significance of the data reported here.



age daily beta neutral ketosteroid excretion comprised 8 to 15 per cent of the average total output. The excretion of adult men (1.2 mg) and that of normal adult women (1.1 mg) were essentially the same, while that of pregnant women (1.9 mg) was, considering the hydrolysis procedure, suggestively higher.

Table 2 gives data on the average daily excretion of neutral ketosteroids by 10 abnormal indi-

TABLE 1 *Average Excretion of Alpha, Beta and Total Neutral Ketosteroids by Normal Subjects\**

TYPE OF SUBJECT	NO. OF CASES	AVERAGE ALPHA NEUTRAL KETOSTEROIDS		BETA NEUTRAL KETOSTEROIDS		TOTAL NEUTRAL KETOSTEROIDS	
		AVERAGE		AVERAGE		AVERAGE	
		mg. per 24 hr.	mg. per 24 hr.	mg. per 24 hr.	mg. per 24 hr.	mg. per 24 hr.	mg. per 24 hr.
Children							
4 to 7 yr.	5	1.2	0.1	0.0-0.2	1.3	0.8-2.6	
7 to 12 yr.	10	3.7	0.3	0.0-0.5	4.0	1.8-5.0	
12 to 15 yr.	7	7.5	0.7	0.0-2.7	8.2	5.0-11.3	
Women 15+ yr.	9	9.1	1.1	0.0-2.5	10.2	6.5-17.4	
Men 15+ yr.	5	13.8	1.2	0.0-1.8	15.0	12.3-18.5	
Women 4 to 7 mo. pregnant	4	13.2	1.9	0.0-4.0	15.1	10.8-20.4	

\*Forty-nine determinations were made on 40 subjects who were hospital staff members or patients presenting no obvious evidence of endocrine disorder.

viduals. Of these, 8 presented definite abnormalities of the secondary sex characteristics, such as a precocious development of the penis to adult

TABLE 2 *Excretion of Alpha, Beta and Total Neutral Ketosteroids by Abnormal Patients*

CASE NO.	ALPHA NEUTRAL KETOSTEROIDS	BETA NEUTRAL KETOSTEROIDS	TOTAL NEUTRAL KETOSTEROIDS
1 Preoperative*	13.0	4.0	17.0
Postoperative (2 yr.)†	17.5	4.5	22.0
2 Preoperative*	29.0	0.0	29.0
Postoperative (4 mo.)†	24.0	4.0	28.0
3	29.0	1.0	30.0
4	45.5	5.5	60.0
5	14.0	1.0	15.0
6	13.8	1.0	14.8
7	9.8	1.4	11.2
8	1.7	0.5	2.2
9	56.0	104.0	160.0
10	83.0	83.0	166.0

\*Preoperative measurements.  
†Measurements made 2 years postoperatively in Case 1 and 4 months postoperatively in Case 2.

size or an abnormally large clitoris, the remaining 2 patients suffered from Cushing's syndrome. Brief summaries of the case reports follow.

CASE 1 (C. H. No. 142513, adrenogenital syndrome). The patient, an 8-year-old boy, was apparently normal until 4 years of age, when his penis began to enlarge and he started to grow rapidly in height. Shortly afterward pubic hair and acne appeared. The history was not otherwise remarkable. On physical examination the patient's general appearance was masculine. He was 61.5 inches in height and weighed 83.5 pounds. The skeletal age was advanced to that for the average 12-year-old boy. The musculature, although well developed, was not excessive. The voice was bass. There was marked acne of the face and thorax. Pubic hair was well developed, and the penis

was of adult size. The testes, however, were of normal size for his age. No spermatozoa were observed in the urethral discharge obtained after prostatic massage. Visual field and eyeground examinations revealed no abnormality. Ventriculoencephalogram showed slightly enlarged lateral and third ventricles. The fourth ventricle appeared to be normal. The blood pressure was 110/60. Intravenous pyelograms showed the left kidney to be rotated slightly away from the midline, a change interpreted as consistent with the presence of a tumor in the region of the left adrenal gland. Dr. Thomas H. Lanman explored both adrenal glands. The right appeared to be normal, the left to be enlarged. The latter was removed and examined by Dr. Sidney Farber. In his opinion there was hypertrophy and hyperplasia of the cortex without evidence of tumor. During the 1st postoperative year there was a temporary decrease in the acne, associated with a temporary fall in the neutral ketosteroid output to half the preoperative level. Two years later, however, there was no striking difference between the preoperative and the existing levels.

CASE 2 (C. H. No. 205690, adrenogenital syndrome). This 11-year-old girl had an enlarged clitoris shortly after birth. At 6 years pubic and axillary hair and minimal acne of the face and thorax made their appearance. At 8 years of age she was 53 inches tall and weighed 62 pounds. At that time she was seen to be masculine in habitus, although her mother reported that she was feminine in behavior. On physical examination marked acne and well developed pubic and axillary hair were evident. In the absence of localizing signs an exploratory laparotomy was performed by Dr. Henry W. Hudson, Jr. An essentially normal uterus and normal fallopian tubes were found. The ovaries appeared to be abnormal. Biopsied specimens of both ovaries were examined by Dr. Farber, who reported that there was a developmental disturbance of the follicles but no evidence of testicular tissue. On re-entry, at 11 years of age, the patient weighed 80 pounds and was 55.5 inches tall. The blood pressure was 110/72. Her general appearance had not changed. The skeletal age corresponded with the average normal for 16 years. Dr. Robert E. Gross explored both adrenal glands and found them slightly enlarged. The right gland was removed and examined by Dr. Farber, who found the cortex to be hypertrophied and hyperplastic but free from tumor tissue. Following the operation there was a temporary improvement in the acne, accompanied by a fall in the urinary neutral ketosteroid output to approximately half the preoperative level. Five months postoperatively there was no definite improvement in the clinical status, nor was there any significant difference between the preoperative and existing ketosteroid output.

CASE 3 (Lab. No. 1, probable adrenogenital syndrome). This 7-year-old girl had a profuse growth of pubic hair and a markedly enlarged clitoris. Laparotomy revealed normal ovaries and a slightly underdeveloped uterus. The right adrenal gland was explored and found to be normal in appearance.

CASE 4 (Lab. No. 2, probable adrenogenital syndrome). This 23-year-old woman had pseudohermaphroditic changes which had been present since childhood. At 10 years of age she was excessively tall and had a low voice. At 11 years she became obese. When seen she presented the chief complaints of primary amenorrhea and hirsutism. Her voice was low and she shaved daily. Mild acne was present. She was obese and had abdominal striae. There was no breast development. The pubic hair had a male

distribution. The clitoris was 2 cm. long. There was apparently a rudimentary vagina. A mass was felt in the left upper quadrant. Periadrenal air injections revealed bilaterally enlarged suprarenal bodies.

Case 5 (C. H. No. 231122 probable combined Addison's disease and adrenogenital syndrome). The case of this 2-year-old boy has been described in detail elsewhere.<sup>16</sup> The outstanding findings included macroglossoma, hyperpigmentation of the nipples and symptoms indistinguishable from those of Addison's disease. Although the penis was very large for the patient's age, the testes were of infantile size. The skeletal age was advanced to the normal for 4 years of age. Intravenous pyelograms revealed no definite abnormalities of the kidneys. The blood pressure was 95/70. The available evidence suggested that the patient was suffering from an abnormality of the adrenal cortex, characterized by persistence and hyperplasia of the fetal type of cortex and underdevelopment of the adult type of cortex a condition similar to that described by Wilkins, Fleischmann and Howard.<sup>17</sup>

Case 6 (Lab. No. 3 Cushing's syndrome without adrenal tumor). This 43-year-old housewife had had 3 normal children. Sixteen years previous to examination she began to feel fatigued and depressed and to have headaches. Two years later the weight increased from 118 to 140 pounds. Two years later the face became plethoric and round. During the last 6 years her previously normal menses had occurred at 2 or 3 months intervals. Five years previously she was given x-ray treatments to the pituitary gland, which relieved the headaches but not the weakness. Shortly afterward ankle edema appeared. In the last 3 or 4 years the weakness had become more marked. On physical examination the patient was obese and plethoric and had abdominal striae. The blood pressure was 130/70. Combined glucose and insulin-tolerance tests showed increased insulin resistance and a glucose tolerance curve of the diabetic type. Roentgenograms revealed osteoporosis of the skull spine and pelvis. The calcium inorganic phosphorus cholesterol nonprotein nitrogen and protein concentrations of the blood serum were normal.

Case 7 (Lab. No. 4 Cushing's syndrome without adrenal tumor). This 26-year-old woman presented obesity hirsutism amenorrhea striae of the skin and headache of 7 years duration. Two years previously both adrenal glands were explored and found to be normal. X-ray treatment of the pituitary gland was given with moderately beneficial results. Shortly afterward the patient developed osteoporosis and renal calculi. An insulin-tolerance curve revealed insulin resistance, a combined glucose-insulin test resulted in a rising blood sugar curve. The basal metabolic rate was -20 per cent. The calcium, inorganic phosphorus, nonprotein nitrogen and protein concentrations of the blood serum were normal.

Case 8 (C. H. No. 236114 masculine precocity associated with adultized testes). This 4-year-old boy showed an increased rate of growth and an abnormally large penis and testes at the age of 3. On physical examination he was 43 inches tall and weighed 62 pounds. The blood pressure averaged 100/65. The musculature was exceptionally well developed and the voice was bass. There was a slight growth of pubic hair but no axillary. The penis and testes were of adult size. Examination of the testis and epididymis revealed no abnormalities. The visual fields were normal. Encephalography showed normal lateral ventricles and questionable enlargement of the third ven-

tricle. The mammillary bodies appeared to be normal. Intravenous pyelograms disclosed no abnormality. The skeletal age was that of a child of 7½ years.

Case 9 (C. H. No. 219534 carcinoma of the adrenal cortex). This 3-year-old girl showed large genitalia and pubic hair at 12 days of age. Acne appeared at 3 months. At about 1 year the clitoris was abnormally large and the voice was deep. At 2 years the patient's size and strength were strikingly above normal. At 3 years she was 42 inches tall and was of male body build. The faces were heavy and the skin greasy. She was not obese. There was abundant pubic hair. The clitoris was markedly enlarged and the labia minora resembled a foreskin. A few vaginal epithelial cells were cornified. A mass was palpable over the right kidney. The bones were heavy, osseous development corresponded to that of a 10-year-old child. Intravenous pyelograms showed the upper pole of the right kidney to be depressed. Dr. William E. Ladd operated and removed a large adrenal tumor. Dr. Farber reported that it was a malignant tumor of fetal adrenocortical origin.

Case 10 (Lab. No. 5 carcinoma of the adrenal cortex). This case of a 13-year-old girl has been described by Friedgood.<sup>18</sup>

Correlation of the excretion data (Table 2) and the characterizations of the patients permit the following comments. The patients with apparent adrenocortical hyperplasia (Cases 1, 2, 3, 4 and 5) excreted approximately six times the alpha, beta and total neutral ketosteroids excreted by normal subjects of corresponding age groups. Two patients (Cases 6 and 7) with Cushing's syndrome excreted normal amounts of alpha, beta and total neutral ketosteroids. A four-year-old boy (Case 8) with enlargement of both testes and penis to adult size excreted only slightly more neutral ketosteroids than did normal children of his age. Two patients (Cases 9 and 10) with carcinoma of the adrenal cortex excreted many times the normal amount of total neutral ketosteroids, abnormally high percentages of which were beta ketosteroids.

## Discussion

Differences in methods of assay make it impossible to compare directly the data presented above with most of the measurements given in the literature. Even so a survey of the literature reveals that the relative levels of total neutral ketosteroid excretion by normal children and adults observed here are in general agreement with the findings of other investigators.<sup>19-24</sup> Normal children below seven years of age excrete negligible amounts of hormone. A definite rise in excretion levels which tended to antedate the appearance of secondary sex characteristics was observed in children between seven and twelve years old. The groups of children reported here are too small to permit observations on the differences in rates of excretion of boys and girls.

Butenandt et al.<sup>27</sup> and Callow et al.<sup>2-5</sup> estimated the beta neutral ketosteroid content of pooled male and female urines by an intricate chemical procedure. They reported that the beta ketosteroids (dehydroisoandrosterone) comprised approximately 10 per cent of the total ketosteroids isolated. The data obtained on normal individuals by the relatively simple and directly quantitative colorimetric procedure employed here compare favorably with these reports, and indicate that the beta fractions comprise, on the average, at least 10 to 15 per cent of the total output.

The elevated excretion of neutral ketosteroids by patients with apparent adrenocortical hyperplasia is in keeping with the increase in capon growth-promoting substances observed in similar patients by other workers.<sup>28-30</sup> The fact that unilateral adrenalectomy was followed by only a temporary fall in neutral ketosteroid excretion and remission in the clinical signs of virilism suggests that the operation is without benefit to such patients.

The two patients with Cushing's syndrome and the boy with adult-sized testes and genitalia were essentially normal, with respect both to total output and to the relation of the alpha and beta fractions.

In contrast to the foregoing, the beta ketosteroid content of the urine from the two patients with carcinoma of the adrenal cortex markedly exceeded the normal values. These high values correspond closely to those observed by other investigators,<sup>8-10</sup> who estimated the beta ketosteroid output by isolating dehydroisoandrosterone or isoandrosterone in crystalline form after extensive purification. Furthermore, the remarkably high output observed in these patients is in agreement with those reports in the literature which are based on biological and colorimetric methods of assay.<sup>18, 31, 32</sup>

Although the available evidence indicates that a markedly elevated excretion of beta neutral ketosteroids is diagnostic of adrenocortical carcinoma, our present experience is not sufficiently extensive to permit the conclusion that a normal or slightly elevated output rules out this diagnosis.

#### SUMMARY AND CONCLUSIONS

With a relatively simple and directly quantitative colorimetric method for assaying the alpha, beta and total neutral ketosteroid content of twenty-four-hour urine specimens, preliminary data defining the average normal rate of excretion of these substances by children of varying ages and by adult men and women were obtained. The rate of excretion of neutral ketosteroids by patients presenting male sex precocity, virilism or Cush-

ing's syndrome (not associated with carcinoma of the adrenal cortex) has been compared with the aforementioned normal rates of excretion. This comparison leads to the following conclusions:

The beta neutral ketosteroids arise solely from substances produced by the adrenal cortex. It follows as a corollary that the rate of excretion of beta ketosteroids may be an index of at least one aspect of adrenocortical activity.

The assay of the alpha, beta and total neutral ketosteroids gives specific information which may be useful in differentiating adrenocortical hyperplasia, Cushing's syndrome without adrenal tumor, and adrenocortical carcinoma.

We are indebted to Drs Fuller Albright and Anne P. Forbes, of the Massachusetts General Hospital, Boston, Dr Gray H. Twombly, of the Memorial Hospital, New York City, and Dr Harry B. Friedgood, of the Beth Israel Hospital, Boston, for urine specimens and case summaries on Cases 3, 4, 6, 7 and 10.

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## THE RELIABILITY OF THE LEUKOCYTE COUNT IN THE DIAGNOSIS OF APPENDICITIS

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THE significance of the total and differential white-blood-cell counts in appendicitis has been debated for more than a generation without any unanimously accepted conclusions being reached. It would seem of interest to subject this problem to some sort of statistical analysis, in the hope of securing factual evidence to replace the vague type of clinical impression which governs many surgical decisions at the present time.

The material studied came from the records of the Springfield Hospital and may be divided into two groups. The 50 cases used as controls consisted of benign and noninflammatory lesions such as strabismus, orthopedic deformities, nevi, lipomas and so forth. All these patients were otherwise healthy and free of infection, and all had normal temperatures, except for 1 child with an unexplained admission temperature of 100°F by mouth, which fell to normal within a few hours. In the second group were 221 cases subjected to laparotomy because appendiceal disease was suspected. These were grouped according to certain arbitrary clinical classifications, which were often the product of retrospective surgical opinion rather than of preoperative diagnosis. The classes were acute appendicitis, acute appendicitis with abscess, acute appendicitis with perforation, acute appendicitis with peritonitis, subacute or chronic appendicitis and mesenteric adenitis. The subacute and chronic cases were grouped because it was found that the distinction between the two represented the purely personal opinion of the surgeon which could not be correlated with the duration of symptoms, physical signs, temperature, white cell count or gross pathology. The original opinion of the pathologist Dr. Fred D. Jones, which was based on the gross lesion, was reduced to simplified terms after discussion with him, namely,

to normal, inflamed and necrotic appendices. The absence of histological study is hardly a serious omission in the acute cases as there is probably no hurry about removing an appendix in which the pathologic changes can be demonstrated only by microscopic study. In the case of the so-called subacute or chronic cases the surgeon may still comfort himself with the reflection that histological study might have revealed changes justifying operation although opinions differ as to how much such observations are likely to alter the opinion of a competent pathologist based on examination of the gross specimen. No attempt will be made in this study to determine the existence of that amorphous entity known as chronic appendicitis, as adequate follow up of the operated cases has not been possible. Without denying that many cases of chronic abdominal pain may be permanently relieved by removing a grossly normal appendix, it has also been found that many such cases were subsequently readmitted because of recurrence of the pain.

The classification according to total white-cell count and percentage of polymorphonuclears requires no explanation. The duration of symptoms was included in the hope that it might help to delineate more sharply the cases listed as chronic or subacute appendicitis. But whereas these cases fell into the classification of weeks, months or years to a greater extent than did the cases diagnosed as acute, there was considerable overlapping.

Before attempting to appraise the clinical significance of leukocytosis and elevated polymorphonuclear percentage it is important to determine the range of normal variations. It is well recognized that this range shifts as the child matures.<sup>1</sup> In this study however the operated cases as well as the controls were distributed over age groups in which the adult range of variations may be

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expected. This range is usually regarded as from 5000 to 10,000 for the white-cell count and from 60 to 70 per cent for the polymorphonuclear distribution.<sup>1,2</sup> An excellent statistical analysis by Medlar,<sup>3</sup> published a decade ago, showed that in an average healthy individual in the course of a few weeks the total white-cell count might vary by 100 per cent and the differential count by 30 per cent without the presence of clinical disease. These variations, moreover, might take place in a given individual in the course of an hour. The least variation encountered was 30 per cent for the total white-cell count and 7 per cent for the polymorphonuclear distribution. Medlar found that a septic leukocyte formula could develop in a normal subject without any clinical evidence of infection. He concluded that the leukocyte mode was 6000 to 9000 for the total white-cell count and 50 to 64 per cent for the polymorphonuclear distribution. In the present study the white-cell count of the control cases was found to have a range from 4300 to 18,600, with a mean of 9286. The standard deviation was  $\pm 3385$ . This gives a normal range, therefore, of 5901 to 12,671. This so closely approximated the textbook normal of 5000 to 10,000 that it was decided to consider a count of 10,000 or more as constituting a leukocytosis. The polymorphonuclear percentage of the controls ranged from 38 to 87 per cent, with a mean of 65 per cent and a standard deviation of  $\pm 11$  per cent. This suggests a normal range of 54 to 76 per cent. It seemed reasonable, therefore, to accept the textbook figure of 70 per cent as the criterion of polymorphonuclear leukocytosis. It is realized that many clinicians consider the total polymorphonuclear count rather than its percentage to be the significant figure. For that reason the cases were also studied in regard to the combination of a total white-cell count of 10,000 or more and a polymorphonuclear percentage of 70 or more. They were similarly studied for the combination of 15,000 or more and 80 per cent or more.

The temperature of 50 control cases showed much less variation, ranging from 97 to 100°F, with a mean of 98.5° and a standard deviation of  $\pm 0.3$ . It was thought, however, that the temperature should be 100°F or more before being considered febrile, since the control cases for the most part represented mouth temperatures, whereas the operated cases varied in the technic of registration.

These rather arbitrary standards of normality having been established, it was decided to study each entity in terms of each of the others. The data bearing on the white-cell count and the poly-

morphonuclear percentage are summarized in Table 1. The complete master table, representing every factor in terms of every other factor, proved to be so cumbersome that it has been omitted for the sake of brevity, and only the pertinent data are included in the following discussion.

The narrow maximum-minimum range of temperature and the small standard deviation in the

TABLE 1 *Total White Cell Counts and Polymorphonuclear Percentages in All Cases*

POLY MOR PHONUCLEAR PERCENTAGE	No OF CASES	UNDER 5000	TOTAL WHITE-CELL COUNT					CN KNOWN
			5000- 10 000	10 000- 15 000	15 000- 20 000	20 000 AND OVER		
%								
Controls (50 cases)								
Under 50	4	0	3	0	1	0	0	
50-60	10	0	8	2	0	0	0	
60-70	19	0	14	4	1	0	0	
70-80	12	1	6	3	2	0	0	
80-90	5	0	2	2	1	0	0	
90-100	0	0	0	0	0	0	0	
Unknown	0	0	0	0	0	0	0	
Totals		1	33	11	5	0	0	
Appendices normal according to pathologist (113 cases)								
Under 50	5	0	4	1	0	0	0	
50-60	15	1	11	3	0	0	0	
60-70	37	0	30	7	0	0	0	
70-80	30	0	18	11	1	0	0	
80-90	18	0	2	10	6	0	0	
90-100	5	0	0	1	3	1	0	
Unknown	3	0	0	2	1	0	0	
Totals		1	65	35	11	1	0	
Appendices inflamed according to pathologist (61 cases)								
Under 50	0	0	0	0	0	0	0	
50-60	3	0	3	0	0	0	0	
60-70	6	1	5	0	0	0	0	
70-80	13	0	10	2	0	1	0	
80-90	19	0	2	6	8	3	0	
90-100	16	0	0	1	9	6	0	
Unknown	4	0	1	1	2	0	0	
Totals		1	21	10	19	10	0	
Appendices necrotic according to pathologist (46 cases)								
Under 50	0	0	0	0	0	0	0	
50-60	0	0	0	0	0	0	0	
60-70	2	0	1	1	0	0	0	
70-80	3	0	0	2	1	0	0	
80-90	20	0	4	5	7	4	0	
90-100	14	0	0	3	3	8	0	
Unknown	7	0	0	1	2	3	1	
Totals		0	5	12	13	15	1	

control group suggested that temperature might be a valuable diagnostic feature, but a study of both clinical and pathological classifications showed very inconstant correlation between temperature and actual severity of the lesion. Of 55 patients classified at operation as having acute appendicitis with abscess or perforation or peritonitis, 22 had normal or subnormal admission temperatures shortly before operation. So also did 63 of the 107 patients whose appendices were classified by the pathologist as acutely inflamed. Conversely, 22 of 113 patients with normal appendices had temperatures ranging from 100 to over 102°F without any other obvious cause. Nor was there any significant correlation between total and polymorphonuclear leukocytosis and febrile tempera-

ture. This seems to lend statistical support to the clinical opinion, held by many experienced surgeons, that the thermometer is of little help in the diagnosis of appendicitis.

Chronic appendicitis showed about the same frequency distribution of febrile cases as did the control group. Mesenteric adenitis was indistinguishable from acute appendicitis so far as the incidence of fever was concerned. The 16 cases of this condition were included in the study inasmuch as exploration was undertaken because of suspected appendicitis and the appendix was actually removed in all but 1 case. None of the criteria studied helped to distinguish mesenteric adenitis from appendicitis. Of the 5 patients with polymorphonuclear distributions of 90 to 100 per cent 2 had acutely inflamed appendices. But of the 2 patients with white-cell counts of over 20,000 one had a normal and the other an acutely inflamed appendix. If we delete these 2 cases of appendicitis, it is evident that mesenteric adenitis may present a clinical picture indistinguishable from appendicitis so far as history, temperature, white

the intensity of the pathologic process in the appendix? Of 127 patients who were suspected of having a diseased appendix and who had a white-cell count of 10,000 or more 79 (62 per cent) had appendices which actually needed removal, as evidenced by the pathologist's diagnosis of acute inflammation or actual necrosis. Of 70 suspects with a leukocytosis of 15,000 or more, 57 (81 per cent) had appendices which needed removal according to the pathologist. Conversely, of 107 patients having appendices with demonstrable gross lesions, 79 (74 per cent) had preoperative white-cell counts of 10,000 or more. Obviously the higher the white-cell count in a case suspected of appendicitis the greater the chance of finding a definite lesion on exploration. But the percentage chance of deviation from this correlation must be appreciated if one is to avoid serious surgical errors from a blind faith in the reliability of the white-cell count. For example 29 per cent of the suspected cases with counts below 10,000 had acutely diseased appendices and 10 per cent had necrotic or ruptured appendices. The constancy of this relation

TABLE 2 Correlation of *Det*

CLASSIFICATION	No. of Cases	Pathologist's Diagnosis	No. Cases	Pr. Ca.
White blood count of 10,000 or more	127	Diseased appendix	79	62
White blood count of 15,000 or more	70	Diseased appendix	57	81
Diseased appendix	107	White blood count of 10,000 or more	79	74
Normal appendix	113	White blood count of less than 10,000	66	58
White blood count under 10,000	93	Normal appendix	65	70
Polymorphonuclear distribution of 70 per cent or more	119	Diseased appendix	85	71
Polymorphonuclear distribution of 80 per cent or more	91	Diseased appendix	69	76
Diseased appendix	10	Polymorphonuclear distribution of 70 per cent or more	57	57
Normal appendix	113	Polymorphonuclear distribution under 70 per cent	57	50
Polymorphonuclear distribution under 70 per cent	68	Normal appendix	57	84

cell count and polymorphonuclear percentage are concerned.

The duration of symptoms was exceedingly variable. They were of comparatively short duration in the cases classified as acute by the surgeon or as actively diseased by the pathologist. This was particularly true of cases with perforation or peritonitis, suggesting that the virulence of the infection rather than neglect or procrastination, was responsible for these complications. Long duration of symptoms predominated in cases classified clinically as chronic or subacute and in those classified by the pathologist as normal. The two were often synonymous. Of 92 cases classified clinically as chronic or subacute, 79 patients were considered by the pathologist to have had normal appendices. And of a total of 113 cases with normal appendices, 79 were found to have been called subacute or chronic appendicitis, 21 acute appendicitis and 13 mesenteric adenitis at the time of operation.

How closely does the white-cell count parallel

may best be measured by a consideration of Table 2. This table also suggests that the differential count is little if any more reliable than the white-cell count as a criterion of either inclusion or exclusion.

When we study the cases suspected of appendicitis with a white-cell count of 10,000 or more and a polymorphonuclear percentage of 70 or more, we find that 68 per cent actually needed appendectomy. If we raise the standard to a leukocytosis of 15,000 or more and a polymorphonuclear percentage of 80 or more we find that nearly 83 per cent needed operation. This would appear to be an exceedingly helpful correlation but it must not be overlooked that 33 (29 per cent) of 113 patients with normal appendices had white-cell counts of 10,000 or more and a polymorphonuclear percentage of 70 or more. Conversely of the 56 cases with both white-cell counts and polymorphonuclear percentages below the critical level of 10,000 and 70 respectively 10 (17 per cent) were

found at operation to have acutely diseased appendices

### SUMMARY AND CONCLUSIONS

In only about 60 per cent of 221 cases suspected of having appendicitis was a total white-cell count of 10,000 or more or a polymorphonuclear percentage of 70 or more indicative of the actual appendiceal lesion found at operation. The combination of the two figures showed a 68 per cent correlation with the pathologist's findings. White-cell counts of 15,000 or more or polymorphonuclear percentages of 80 per cent or more were considerably more reliable, but to have demanded such figures as a criterion for operation would have resulted in neglecting a correspondingly greater number of acutely diseased appendices. The same criticism applies to demanding a white-cell count of 15,000 or more *and* a polymorphonuclear percentage of 80 or more. This combination occurred

in 83 per cent of the cases with diseased appendices, but also in 9 per cent of the cases found to have normal appendices. This attempt to measure the reliability of the white-cell count in appendicitis in terms of the percentage chances of error should not be construed as vitiating the usefulness of the procedure. Rather it is a plea not to trust blindly to a low white-cell count as conclusive evidence against appendicitis, nor to a high one as overwhelming evidence in favor of operation.

I am indebted to Dr Herbert L. Lombard, of the Massachusetts Department of Public Health, for advice and suggestions in regard to the statistical analyses.  
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## REPORT ON MEDICAL PROGRESS

### CLINICAL NEUROLOGY

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**D**URING the past year, a number of important subjects have come to the attention of clinical neurologists or have developed which might be dealt with here, but which have been or will be considered in other progress reports. For example, the use of sulfanilamide and similar preparations has changed our attitude toward intracranial infections, in particular meningitis. Also a consideration of muscle disorders, presented last year, may well be covered in a later report embodying physiological, chemical and clinical advances in this ever-changing field. Subjects of neurosurgical interest have also been covered under a separate heading. The same applies to a large number of diseases and conditions of the nervous system now recommended for vitamin therapy of one form or another. Again, the fundamental consideration of vitamins had better rest with specialists for the present, and clinical advances in this field be reported when the basis for such treatment has become less nebulous. There remain, however, a number of topics of varied interest to the clinical neurologist.

### LAW OF DENERVATION

Cannon<sup>1</sup> has amassed evidence from his own experiments and many numerous earlier observations which he sums up under a "law of denervation," expressed as follows: "When in a series of efferent neurones a unit is destroyed, an increased irritability to chemical agents develops in the isolated structure or structures, the effect being maximal in the part directly denervated."

The evidence is most conclusive in connection with the autonomic nervous system, in which denervation of smooth muscle by interrupting its postganglionic, ganglionic or preganglionic supply leads to overreaction. An example cited is the "paradoxical pupillary reflex" if the dilator fibers of the iris are cut the pupil becomes small, but under certain conditions, such as fright or the injection of adrenalin, the pupil not only dilates but does so more than the pupil of the normal eye. Another example, of clinical significance, is the increased sensitivity to adrenalin of blood vessels denervated because of Raynaud's disease. Skeletal muscle is subject to this law. For example, a paralyzed facial muscle may be made to contract by the injection of acetylcholine. Glands

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also follow the law, as shown by experiments on the submaxillary and lachrymal glands

Not only does the law of denervation hold for the peripheral nervous system, but experimental evidence is offered which suggests that a lesion of the spinal cord may also sensitize the appropriate neurones to overactivity. Cannon even postulates a similar situation in the cortex and asks, "Is it not possible that tumors, and such lesions of the motor area of the cortex as are associated with the name of Hughlings Jackson, may induce instability of the neighboring cortical cells by destroying their connections with other cortical cells?" Cannon's report, based on physiologic evidence, contains numerous suggestions for clinical adaptation in explaining different types of irritability of the nervous system.

#### VERTEBRAL VEINS AND METASTASIS

Batson<sup>2</sup> offers anatomical evidence to explain routes of infection and tumor metastasis hitherto inexplicable. By means of injections into human cadavers and living monkeys, he showed that veins ordinarily considered as draining into the inferior vena cava also connect with the vertebral veins, and these in turn connect with cerebral sinuses. He believes that this system of vertebral veins forms a by-pass which may under certain conditions such as coughing, straining and so forth, admit blood directly from the caval system. He thus explains brain metastasis without lung involvement or an open foramen ovale. While I am not qualified to judge of the reliability of the methods employed by Batson, he seems to supply a long needed anatomical explanation for certain metastases to the brain and spinal cord, hitherto quite unsatisfactorily accounted for.

#### HIPPOCAMPAL HERNIATION

Considerable attention has been given to herniation of the cerebellum into the foramen magnum, with associated flattening of the medulla against the basilar portion of the occipital bone. This is seen especially with tumors in or about the cerebellum and is a frequent cause of death. Furthermore, when such a hernia is imminent, it is facilitated by lumbar puncture or withdrawal of spinal fluid from any point below.

Herniation of the brain through the tentorium and its effect have received less recognition. This is caused by an expanding lesion above the tentorium which slowly forces the hippocampus of the temporal lobe into the incisura tentorii. In so doing it causes pressure on the midbrain and may cut off the basilar cisternae, resulting in a partial fluid block between the forebrain and the brain stem.

As in foraminal herniation, withdrawal of spinal fluid facilitates the incisural herniation. Schwarz and Rosner<sup>3</sup> give the symptomatology of hippocampal herniation as follows: fluctuation in the state of consciousness, anisocoria, with or without dysfunction of the pupillary light reflex, nuchal rigidity, imbalance of extraocular muscles, cardio-respiratory and thermoregulatory disturbances, paradoxical and shifting signs of involvement of the pyramidal tracts and decerebrate rigidity. These symptoms are best explained by compression of the brain stem and dislocation of the brain stem was frequently found by these investigators when the herniation was on one side only.

Reid and Cone<sup>4</sup> lay stress on two results of supposedly direct pressure from the hernia. They believe that the dilated and fixed pupil seen in generalized increased intracranial pressure is due to direct pressure on the third nerve as it passes through the incisura. Not only do they argue from clinical evidence alone but in experimental observations in monkeys they were able to cause dilatation of the ipsilateral pupil with increased extradural pressure and to see the dilatation disappear on reduction of pressure. These authors also noted thrombosis of the occipital lobe on the same side as the hernia and explain this on the basis of direct hernial pressure on the posterior cerebral artery. In this connection it will be remembered that Leary and others have stressed unilateral dilatation of the pupil as indicative of the side on which subdural hematoma occurs.

Both Schwarz and Rosner and Reid and Cone discuss a mechanical state occurring in elevated cerebral pressure which should be recognized by the neurologist before too late. In dealing with the condition Fay in his discussion of Schwarz and Rosner's paper states that resection of the tentorium in the neighborhood of the hernia is indicated and in his experience is a satisfactory procedure.

#### HEADACHE

Pickering<sup>5</sup> analyzes several types of headache, and concludes that stretching of cerebral arteries is the common etiologic factor in headaches caused by histamine, following lumbar puncture and in hyperpyrexia, migraine, brain tumor and meningitis. In histamine headache the immediate response is a rise in cerebrospinal fluid pressure, accompanied by a drop in systolic blood pressure and by flushing of the face. The second stage is a drop in fluid pressure and rise in arterial pressure and it is at this time that the actual headache comes on, lasting approximately eight minutes.

Horton MacLean and Craig<sup>6</sup> thus describe a type of headache occurring chiefly in middle life



The pain of which the patients complained was limited to one side of the head. It was a constant, excruciating, burning, boring type of pain which involved the eye, the temple, the neck and often the face. It had none of the tic-like qualities of trigeminal neuralgia, and there were no trigger zones. There was frequently marked tenderness on pressure over the branches of the external carotid and common carotid arteries. The bouts of pain appeared and disappeared very quickly. The onset and cessation frequently could be measured in minutes. The duration of the headache varied from fifteen minutes to several hours. In most cases the headache occurred with clock-like regularity, particularly at night, the patients awakening with pain night after night and week after week at a certain hour. Although night pain was characteristic, pain during the waking hours was common. Remissions and exacerbations in many cases occurred spontaneously.

In 25 such cases the typical attack could be reproduced by the subcutaneous injection of 0.3 to 0.5 mg. of histamine. In 20 of these cases the histamine-induced attack could be completely controlled by the intravenous injection of epinephrine and other vasoconstricting agents, and spontaneous attacks could be controlled in a similar manner. The treatment affording relief in 65 cases was the giving of increasing doses of histamine. The dosage began with 0.05 mg. given subcutaneously twice daily for two days, on the third day it was increased to 0.066 mg. and by the fifth day to 0.1 mg., which was administered twice daily for the next two or three weeks. These authors suggest that this type of headache be called "erythromelalgia of the head."

Penfield and McNughton<sup>7</sup> have been studying the mechanisms of intracranial pain for a number of years and have now published an amplification of their previous reports, covering the anatomical study of the nerve supply of the dura and the clinical experience that corroborates their conclusions. For the clinician it will suffice to state that dural innervation is found especially about the meningeal blood vessels, and that above the posterior fossa the nerve supply comes from the trigeminal nerve on each side. It is of particular interest that the first branch of this nerve is chiefly concerned, supplying the sensitive longitudinal sinus anteriorly through ethmoidal nerves, and posteriorly through a recurrent branch (tentorial nerve) originating as far forward as the cavernous sinus. A number of detailed and carefully checked case reports are chosen to confirm the conclusions as to points of origin and regions of reference of intracranial origin. Here is a new conception of the pain mechanism, contrasted with that of previous authors. Penfield and McNughton assert, "lost head pain must be dural in origin." "The origin of 'dural' must be in the dural sinuses and

the veins tributary to the sinuses in their course across the subarachnoid space from the brain. The response to stimulation of the dura was always pain, whether the stimulus was pressure, traction, heat or electric current. They find the brain itself insensitive, and also the walls of the ventricles, a conclusion contrary to some previous ones. Certain brain cicatrices are painful. These clinical observations agree with the anatomical stressing the importance of the first branch of the trigeminal nerve as the principal nerve mediating pain in the head.

Von Storch, Secunda and Krinsky<sup>8</sup> have sought by means of small injections of air by the lumbar route, directed to different places in the ventricular subarachnoid system, to estimate points at which headache is produced. Needless to say, the location of the air is checked by x-ray examination. As little as 2 cc. of air, not enough in their opinion to produce pressure change, causes headache, especially when placed in the basilar cisternae. They also conclude that the walls of the lateral ventricle are insensitive to air injection.

#### THE HYPOTHALAMUS

Many papers concerning the hypothalamus have appeared in the last few years. A book by Clendinning et al.<sup>9</sup> and finally a symposium under the auspices of the Association for Research in Nervous and Mental Disease,<sup>10</sup> together with a series of lectures by Dr. Stephen W. Ranson at the Harvard Medical School in the spring of 1940, have brought out many important aspects of this subject.

To the clinician, the anatomy of this small region of the brain above and immediately posterior to the hypophysis is bewildering. It is a phylogenetically ancient area, grossly not circumscribed but containing six regions, each with two or more nuclear masses. It has a very rich blood supply. Its anatomic connections are numerous and not yet verified, but fiber connections with the infundibular stalk and the hypophysis, and with the thalamus and with the midbrain, are assured.

Physiological differentiation of the nuclear masses and fiber connections is extremely difficult because of the site of the hypothalamus, its small size and the close apposition of its various components. While many functions of the body are controlled by interference with this region, it is certain that function originates there. Although its connections with other portions of the brain and with glands of internal secretion, particularly the hypophysis—the hypothalamus exerts control over sympathetic activities of the body. No other function has been suggested.

reviewing the physiological and clinical evidence one may formulate two groups of influence at tributary to hypothalamic dysfunction. The hypothalamus is of major importance in temperature regulation, regulation of blood pressure, pilomotor response, water metabolism, fat metabolism and deep it is of relative importance in sugar metabolism, sexual behavior, gastrointestinal motility and lesions, somatic response, emotions and personality.

Fulton<sup>11</sup> summarizes the clinical syndromes of the hypothalamus as five in number:

Hypothermia (posterior nuclei) hypersomnia (posterior nuclei and mammillary bodies) the adipogenital syndrome with disturbed fat and carbohydrate metabolism (tuber cinereum) diabetes insipidus (supraoptic nuclei) generally accompanied by hyperthermia and autonomic epilepsy caused by tumors, infection or intraventricular drugs with manifestations varying with the site of the lesion and involving a mixture of sympathetic and parasympathetic actions. The posterior hypothalamus contains predominantly sympathetic representation in the middle and anterior nuclei predominantly parasympathetic, and the functions integrated clearly involve both systems. But all levels of the hypothalamus are subject to regulation from thalamic, striatal and cortical levels.

Perhaps for the present clinicians should, in the words of Foster Kennedy, consider the hypothalamus as "a neuroglandular instrument in command of vital rhythm."

Erickson<sup>1</sup> defines neurogenic hyperthermia as follows:

The clinical picture is dramatic. Most striking is the rapid rise of rectal temperature, the relative warmth of the trunk and the icy dryness of the extremities. Venous blotching often appears in non-dependent portions of the skin of the extremities and less frequently in the trunk. Piloerection may be present, and there is complete absence of sweating (anhidrosis). Thus it is evident that heat loss is reduced to a minimum as there is no sweating and blood flow in the skin of the extremities is greatly reduced. The patient is quiet, practically never agitated and almost always unconscious.

Neurogenic hyperthermia, according to this writer usually follows operation in the neighborhood of the hypothalamus within twelve hours. Once it is established the patient is likely to die, but when its onset is suspected prophylactic measures may be of great value. These measures are directed to causing heat loss through the skin and slowing of the heart rate. Although very high temperatures have been recorded the diagnosis does not depend on this point and Erickson considers such temperatures as an indication of poor appreciation of the situation by doctor or nurse.

#### "BULGARIAN TREATMENT"

The demand for treatment for Parkinson's disease is apparently increasing. Drugs of the

atropine series are often of value, sometimes worthless and sometimes toxic. The usual procedure is to try one after another in an attempt to find the best drug or the best combination of drugs for the given case.

For some time the original Bulgarian belladonna has been heralded as by far the best drug—especially perhaps because the supply was precarious. Possibly Vollmer<sup>12</sup> has settled the matter for us. He has used various preparations of belladonna in the treatment of the Parkinsonian syndrome, and has analyzed them. He concludes that there is no secret remedy and that success is not dependent on unknown impurities. The original Ræff's Bulgarian root was found not to be duplicated by other Bulgarian roots, and conversely he found some American roots as potent as the original Bulgarian. He therefore postulates a synthetic formula which in his present opinion is best. It consists of 90.2 per cent hyoscyamine hydrobromide, 7.4 per cent atropine sulfate and 2.4 per cent scopolamine hydrobromide. The average daily dose for postencephalitic Parkinson's disease is 3.30 mg., and that for paralysis agitans 1.86 mg.

#### LIGAMENTA FLAVA AND LOW BACK PAIN

Herniation of an intervertebral disk as one cause of low-back pain with sciatic radiation must now be considered as an accepted fact. In operating on such cases it was occasionally noted that a thickened ligamentum flavum accompanied a ruptured disk, and it was not long before an occasional case operated on for herniated disk failed to show this lesion, but did show a thick ligamentum flavum.

This ligament is a paired structure connecting the laminae throughout almost the entire extent of the spine. It contains chiefly yellow elastic tissue and is capable of considerable stretching. The significant fact is that its lateral attachment forms part of the intervertebral foramen hence enlargement of this ligament from any cause narrows the foramen and impinges on the nerve root. This is especially true of the lumbar region. A thorough investigation of this subject was conducted by Naffziger, Inman and Saunders<sup>13</sup>; they consider hypertrophy of the ligamenta flava as another important cause of so-called "sciatic pain."

Brown<sup>14</sup> has investigated considerable literature on the subject. The normal thickness as reported is variable, —2 to 7 mm (Spurling<sup>15</sup>), 2 to 4 mm (Dockerty and Love<sup>17</sup>), —with pathological figures of 10 to 16 mm and 2.5 to 9.5 mm., respectively. It is therefore evident that thickening may be very considerable. Evidence for establishing this thickening on an intrinsic pathological basis is lacking and the process is generally considered

one of hypertrophy, and the etiology trauma. X-ray studies are negative except where contrast mediums are used, and even with Lipiodol the best interpretation may not discriminate between a ruptured disk and a hypertrophied ligamentum flavum.

It might perhaps be of academic interest to discuss at length the differential diagnosis between these two conditions, for usually the localization is accurately obtained, and operation is directed in the same manner for both conditions. However, it seems possible that without operation the prognosis in the case of a resilient hypertrophied ligament might well be better than in that of a firm, protruded disk.

#### WERNICKE'S ENCEPHALOPATHY

Encephalopathy, originally described in 1881 by Wernicke, has usually been considered as rare. Its etiology has been obscure, although alcohol has been regarded as the exciting agent or at least an accompaniment. Its treatment is unsatisfactory. It has been for years spoken of as *polioencephalitis hemorrhagica superior*, a term connoting that it is an inflammation of the gray matter of the brain analogous with *poliomyelitis*. Recent investigations have helped to a better understanding of this condition.

Briefly the disease is characterized by paralysis of various eye muscles, pupillary changes often simulating the Argyll-Robertson type, a reeling gait, disturbances of consciousness and personality changes characteristic of Korsakow's psychosis. Somnolence, tachycardia and disturbances of respiration are frequent. The disease usually runs an acute or subacute course ending in death.

Campbell and Biggart<sup>18</sup> have collected 12 cases proved by autopsy, and have made clinical and pathological observations of great value. Their pathological findings uniformly showed vascular changes in the subcapillaries, mostly in the gray matter, with a predilection for the corpora mammillaria, thalamus, anterior and posterior colliculi and periaqueductal gray matter. The lesions, usually visible to the naked eye, consisted of minute hemorrhages, fragile vessels and a glial reaction. There is no evidence for inflammation, and nerve cells in areas affected remain relatively unaffected. The chief interest of these authors' contribution lies in their discussion of etiology. The cases were all derived from a general hospital, none from mental hospitals, and only 1 was definitely alcoholic. Two patients were pregnant and had vomited, and, most important, 5 had markedly abnormal gastrointestinal tracts (3 gastric carcinoma, 1 an old gastroenterostomy, 1 a bowel resection for tuberculosis). Campbell and Biggart consider the three most likely theories of causation: alcohol, some toxic agent and lack of vitamins. Neither their

cases nor most reports in the literature confirm alcohol as a direct cause, the toxic theory, as advanced by Neuburger, does not satisfy them, lack of vitamin B<sub>1</sub> is the only common denominator which to them seems present or probable in their cases, yet they suspect that some other factor, perhaps an endotoxic one, is contributory.

Ecker and Woltman<sup>19</sup> come to a similar conclusion, namely, that there is a deficiency of vitamin B, and perhaps vitamin C, but it must be admitted that the evidence given is not highly satisfactory.

In this connection some experimental work by Alexander, Pijoan and Myerson<sup>20</sup> is contributory. These workers were able to produce the lesions of Wernicke's disease in pigeons by withholding vitamin B<sub>1</sub> but not by withholding vitamin C.

\* \* \*

In closing this review it is fitting to comment on a new textbook on neurology written by the late S. A. Kinnier Wilson<sup>21</sup>. This is a two-volume work representing the ideas of a single great neurologist, except for necessary posthumous editing by A. Nimian Bruce. It thus follows, without superseding, the valuable works of Gowers and Oppenheim.

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., Editor

## CASE 26361

### PRESENTATION OF CASE

*First Admission* A seventy-one year-old white married Newfoundland carpenter was admitted complaining of pain in the back.

Two and a half years prior to admission the patient fell from a house a distance of 25 feet landing on his back. He was unconscious for about two hours and remained in bed for a few days, following which he returned to work and felt well except for slight discomfort in the upper dorsal and lower cervical regions of the spine. This discomfort soon disappeared. He continued working and felt normal except that the pain occasionally returned, especially on looking upward, forcing him to stop work for one or two hours. Two months before entry the pain became much worse and gradually increased. He could not lie on either side, and after sleeping for about three hours it was necessary for him to sit up to get relief. The pain was aggravated by almost all movements of the neck. It frequently radiated down both arms. It was worse on coughing and sneezing. For many years he had had "stomach trouble," which consisted of gas and belching but no pain. He used laxatives frequently. There were no chest or urinary symptoms, and he had not lost weight. He had been usually well all his life prior to the onset of the present illness. His family history was non-contributory.

Physical examination showed a well-developed, thin man who appeared younger than his stated age. Examination of the head was negative. The neck showed no enlarged lymph nodes; the veins were not distended. Examination of the chest was negative. The blood pressure was 140 systolic, 90 diastolic. The abdomen was slightly distended. There were no palpable organs, masses or tenderness. Rectal examination was negative. The back of the spine was tender over the first and second dorsal vertebrae. Movements of the neck caused pain. His strength was normal in both arms. Neurological examination was negative.

The temperature was 97.4°F., the pulse 74, and the respirations 18.

Examination of the urine showed a specific gravity of 1.029, a trace of albumin, no sugar.

rare granular and a few hyaline casts, and an occasional red cell and 3 white cells per high power field. The hemoglobin of the blood was 85 per cent. The serum protein was 7.4 gm per 100 cc. A sputum examination was negative for acid fast bacilli. A Bence-Jones protein test showed slight cloudiness by the heat test at 70 to 80°F.

X-ray films of the cervical and upper dorsal spine showed slight narrowing of several of the upper dorsal vertebrae with slightly increased dorsal kyphosis, slight scoliosis and osteoporosis. There was marked spur formation between the fifth and sixth cervical vertebrae. X-ray films of the skull were negative. A gastrointestinal series was negative. X-ray films of the chest showed that the lung fields had a mottled appearance, small areas of dullness outlining the lymphatic structure of almost the entire lung field. The left ventricle was somewhat blunted and slightly prominent; the aorta was tortuous and calcified.

After entry it was found that the patient had a chronic cough which he said was due to catarrh. A son stated that his father's face had been getting thin; this was attributed to the fact that the patient could not eat anything because of stomach trouble. An orthopedic consultant found that the head and neck showed marked limitation of motion during flexion, extension and rotation. There was no localized tenderness over the cervical vertebrae, and examination of both shoulders was entirely negative for limitation of motion. Examination of the upper back region showed localized tenderness over the rhomboid muscles and over the fourth and fifth dorsal spinous processes. The tenderness was like that of a myositis. Motions of the spine did not seem to affect this pain appreciably although the patient stated that holding the shoulders back had a tendency to relieve it somewhat. The patient was discharged on the day of admission to return shortly for further study and treatment.

*Final Admission* (one month later) Since the last admission the patient had eaten very little and had failed rapidly. No new symptoms had developed except that the cough had become more prominent. It was of a repeated hacking nature, with little sputum. The spinal pain had decreased in severity.

Physical examination showed the patient to be very uncomfortable with an almost constant cough and dyspnea. There was slight cyanosis of the lips. He appeared anemic and showed evidence of recent weight loss. Examination of the neck was unchanged. Examination of the chest showed weak breath sounds with coarse and fine rales throughout, more marked on the right. The coarse rales were usually heard best at the end of ex-

piration. No tubular or cavernous breathing was noted. There was dullness over the right lower lung field posteriorly. The heart sounds were of poor quality. A systolic murmur was heard at the apex. The blood pressure was 120 systolic, 70 diastolic. Examination of the abdomen was negative. The extremities were normal. Neurological examination was negative.

The temperature was 100°F, the pulse 80, and the respirations 30.

The urine showed a trace of albumin. A Bence-Jones protein test was negative. The blood showed a red-cell count of 3,830,000 with 70 per cent hemoglobin, and a white-cell count of 14,200 with 84 per cent polymorphonuclears, 12 per cent small lymphocytes and 4 per cent mononuclears. The smear showed moderate achromia, the platelets were increased.

X-ray examination showed moderate hypertrophic changes about the margins of the bodies of the cervical and dorsal vertebrae. The right scapula was definitely abnormal in structure about the glenoid, the appearance suggesting bone destruction with a pathologic fracture.

On the third hospital day the patient suddenly slumped on the stretcher while in the x-ray department. He immediately became cyanotic and moribund. The pulse was weak, although the heart beat remained fairly regular. He did not respond to stimulants and died twenty-five minutes later.

#### DIFFERENTIAL DIAGNOSIS

DR AUBREY O HAMPTON. I am having some difficulty in finding the pathologic fracture and the bone destruction in the scapula. It may be that I have not the right films, but I assume that it was from this film here that the description was taken. It does look abnormal, but I do not think I should go quite so far as to say there is a fracture. Here, in one of the lateral films, you can see the scapula near the glenoid, and it looks as if there is a round area of destruction. The most marked changes are in the chest and upper dorsal vertebrae. There are wedge-shaped vertebrae at the fifth and ninth dorsal areas. There is no paravertebral tumor. The outlines of the vertebrae are quite smooth. The chest findings are very unusual.

DR EARLE M. CHAPMAN. There is nothing said about the man's occupation except that he was a carpenter. We do not know whether he was exposed to silica. This is not consistent with silicosis?

DR HAMPTON. No, there is a diffuse process in both lungs without gross enlargement of the hilar markings. The appearance is that of plaque-like areas of density perhaps around the lymphatics

and around the bronchi, more like diffuse cancer than anything else, possibly due to fibrosis here on this side, but the lymph nodes were not enlarged.

DR CHAPMAN. This man came in again one month after this picture was taken, and the film showed definite signs in the chest, particularly at the right base, of what appears to have been consolidation. There was dullness over the lung field, which might have been due to fluid. This is a puzzling situation, but it seems to me that he must have had a diffuse carcinomatous process to account for his death, which was rather dramatic and, I take it, unexpected. He apparently had diffuse involvement of the bone and bone marrow, leading to stimulation of the marrow. We find that he had an increased number of platelets, an elevated white-cell count and an anemia, and at the second entry, after he had begun to lose weight, he had the signs of a pathologic fracture. The first positive laboratory finding was the report of Bence-Jones protein, yet there was no increase of serum protein and no typical plasma cells in the blood smear. One can frequently find a slight amount of Bence-Jones protein in the urine of patients with carcinoma that involves the bone marrow. He had a large amount of albumin in the urine, and that is difficult to explain. He might have had Bright's disease, but with a specific gravity of 1.029 it seems as though the renal function must have been good. There was an occasional red cell in the urine. The one thing we know is that this man for years had had stomach trouble, — gas and belching, — and again at the second entry we find that his stomach had gone back on him. A son said that the patient could not eat anything and that he had become progressively worse, and yet the gastrointestinal series was negative on the first entry.

Where did this cancer arise? It is going to be extensive in the bone and bone marrow, and also more extensive in the lung than indicated by x-ray study, especially at the right base, possibly with destruction leading to an abscess cavity. Apparently, as a final episode, he must have had a fracture of a cervical vertebra causing cord compression and sudden death. A primary tumor of a vertebra is a possibility, however, there is little to indicate it in the history. He might have had a primary tumor in the stomach that was missed by x-ray. I shall discount it and say it was not there because the gastrointestinal series was negative. It might have come from the liver. It is known that hepatoma metastasizes to bones very extensively. Bolker, Jacobi and Koven\* reported

\*Bolker, H., Jacobi, M., and Koven, M. T. Primary carcinoma of the liver with bone metastasis. *Ann. Int. Med.* 10:1212-1221, 1937.

a series of such cases three years ago, pointing out that pathologic fractures and bone metastases can occur without evidence to indicate a primary hepatoma.

I do not suspect the pancreas as the source of the tumor. We have no record of pain in the lumbar region, the back pain was higher. I doubt that it could have arisen in the lower bowel, because of the absence of any symptoms suggestive of obstruction. Were the kidneys involved? Could it be primary hypernephroma involving one kidney or the other, with no localizing symptoms or signs? We know that primary kidney tumors metastasize freely to the lungs and also to bone.

I can only say that the man had widespread cancer involving the marrow. I think the presence of Bence-Jones protein was due to carcinoma in the marrow and not to multiple myeloma. If I had a choice, I should say, first that it was primary in the liver, and second, in the kidney.

DR. CHARLES L. SHORT: We saw the patient first in the diagnostic clinic, and he presented a picture much as has been outlined. We suspected he had cancer but were quite unable to demonstrate it. At that time the x-ray films of the spine were interpreted as showing only changes due to degenerative arthritis, and the lesions in the lungs were said to be undoubtedly due to fibrosis. We could not talk the radiologists into making a diagnosis of cancer on the chest plate. When he was re-admitted he looked even more like a patient with cancer. He had gone downhill tremendously, and unfortunately died before the x-ray reports came back—so we still had only a probable diagnosis of cancer.

DR. HAMPTON: The pulmonary findings are unusual for metastatic cancer but we have seen similar ones notably in cancer of the pancreas.

#### CLINICAL DIAGNOSES

Pulmonary fibrosis  
Carcinoma of lung?

#### DR. CHAPMAN'S DIAGNOSES

Carcinomatosis with metastases to lung and bone marrow  
Primary liver cancer?

#### ANATOMICAL DIAGNOSES

Colloid adenocarcinoma of head of pancreas, with metastases to liver, lungs, bronchi, cisterna chyli, lymph nodes and cervical vertebrae.  
Tumor emboli, pulmonary arteries

Obstruction of thoracic duct and cisterna chyli with chylous ascites  
Pulmonary tuberculosis healed, apical  
Nephritis, chronic vascular

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This man had widespread carcinoma including involvement of several vertebrae and a rather extensive extradural growth in the spinal canal. We did not find any factor definitely to explain the precipitate character of his death. There was no fracture of the cervical vertebrae. On the other hand the intra-spinal growth may well have produced pressure on the cervical cord and medulla. The primary source of the tumor was in the pancreas. The head of the pancreas, as you undoubtedly remember is in two sections, one of which is continuous with the body and tail and is drained by the duct of Wirsung. The other is intimately attached to it but has a separate duct. The cancer in this case was limited to the portion of the pancreas drained by the duct of Santorini which did not enter the papilla of Vater. For that reason no jaundice was present. The cancer was quite small, less than 3 cm. in diameter. The lungs showed mostly metastatic tumor, but there were some areas of fibrosis due to an inactive, almost healed tuberculosis.

#### CASE 26362

#### PRESENTATION OF CASE

A seven month-old female infant was admitted to the hospital because of vomiting of a few hours duration.

The patient seemed entirely well the day before admission. She took feedings at normal times and in normal amounts. She slept until 1 a.m. the day of admission when the mother was awakened by the child moaning. The infant felt hot, was restless and began to vomit. She vomited on four separate occasions until 6 a.m., when she was able to take an ounce of water without emesis. The child continued to be restless and feverish and at 8 a.m. a "red mark" appeared under the chin. After two more similar discolorations had developed the mother called a physician who advised immediate hospitalization. No diagnosis was given at the time. There had been no cough, convulsions or evident weakness. Two weeks before admission, the child had had a cold with cough lasting five to six days, but since that time she had appeared to be well. She had one stool on the morning of admission, and urination occurred once.

The past history revealed that the infant had been a full-term normally delivered baby, breathing occurred immediately, without artificial respiration. The child was formula fed, and at the time of entry was receiving milk (1 quart), water (4 ounces) and Karo (3 teaspoonfuls), strained vegetables, cod-liver oil and Pablum were taken daily. The child had received no orange juice or other fruit juices, as these had been vigorously refused. She gained in weight normally and was seen in the Well-Baby Clinic on numerous occasions. There had been no prophylactic serum inoculations. The infant had had no previous illnesses. The family history was non-contributory, there were five older siblings, the oldest being fourteen, and none of these had been sick, the parents were living and well.

Physical examination revealed a well-developed and well-nourished infant who lay on its back, rolling slightly from side to side and crying continually. The entire skin was stated as being "amazing." There were large areas of blotchy, reddish-black discoloration that blanched with pressure, and remained thus for many seconds after the finger had been removed. Scattered over the body were numerous, palpable but macular hemorrhagic spots, measuring up to 0.3 cm in diameter. These areas developed under observation and in the course of two hours, twenty to thirty were counted, they occurred without apparent relation to points of pressure or trauma over the body. Except for the skin lesions and a dusky cyanosis of the mucous membranes of the lips, eyelids and nail beds, the physical examination was negative. There were no purpuric spots in the mouth or pharynx. The throat and tonsils were pale.

The temperature was 102.8°F, the pulse 100, and the respirations 32.

Examination of the blood showed a red-cell count of 3,800,000. A white-cell count was 30,000, with 21 per cent polymorphonuclears, 2 per cent large lymphocytes, 69 per cent small lymphocytes, 2 per cent monocytes and 1 per cent eosinophils. The smear showed normal red cells with very few platelets, there were many disintegrating polymorphonuclear cells. The platelet count was 81,000. A gram stain of the blood smear was negative for intracellular diplococci. The bleeding time was 2 minutes. A lumbar puncture showed normal dynamics, and the spinal fluid contained 300 red cells and 8 white blood cells per cubic millimeter, with a total protein of 14 mg per 100 cc and a sugar of 36 mg.

The child quickly failed, and died two hours after admission.

## DIFFERENTIAL DIAGNOSIS

DR RICHARD C TEFFT This case presents a picture which is absolutely typical of the Waterhouse-Friederichsen syndrome. Indeed, were it not for the discrepancy of a month in age and a mere matter of a difference in sex, it might well be a description of the original case published by Waterhouse, which gives the syndrome a portion of its name. Because the picture is so typical, the differential diagnosis can be very brief.

Certain drugs can cause symptoms somewhat similar, but aside from the fact that self-administration would be practically impossible in a child of this age, any drug which could cause this picture would have produced symptoms much sooner after ingestion — the baby had been asleep presumably from seven o'clock in the evening until one o'clock in the morning. Scurvy could not produce this picture without a preliminary history of the symptoms of subperiosteal hemorrhage, which are so dramatic, together with blood in the urine and spongy, bleeding gums. Acute leukemia might produce the picture, but while this disease sometimes results in an early fatality, it would not be so fulminating as this was and the red count was altogether too high for a leukemia that had been going on for only several days. In the past, when diagnostic methods were not so far advanced as they are at the present time, fulminating purpuras were described. In all probability most of these were cases similar to the one under consideration and not uncomplicated thrombocytopenic purpura. For an uncomplicated purpura to produce death as rapidly as this, the *modus operandi* would have to be hemorrhage, which is specifically denied in the history of this case. An overwhelming infection of one sort or another is frequently the cause of sudden death in infancy. It kills as rapidly as this, and indeed, I think there is no doubt that this is one type of overwhelming infection.

The only feature in this case which is not absolutely typical of the Waterhouse-Friederichsen syndrome is the lymphocytosis. Usually there is either a polymorphonuclear leukocytosis or a normal white-cell count — occasionally leukopenia. I think the lymphocytosis in the present case can be explained on the basis of a fulminating infection that overwhelmed the bone marrow. As frequently happens in infancy where the response of the tissues supplying white cells to the blood stream is not so sharply differentiated as it is in adults, the baby unable to supply granulocytes to fight infection does the best he can with lymphocytes.

The Waterhouse-Friederichsen syndrome is

characterized by sudden onset, extraordinary purpuric manifestations, collapse, coma and death. At autopsy in every case, massive hemorrhage into the adrenal glands is found. In the earlier reported cases no definite causative agent emerged. In the last ten years, however, in more than half the cases the meningococcus has been grown from either the blood stream, the petechial spots or both. Occasionally a hemolytic streptococcus or a pneumococcus has been reported. I should expect in this child the very numerous petechial hemorrhages would point to an organism in the blood stream very probably a meningococcus. These petechial hemorrhages are really small infected thrombi, and the organism frequently can be recovered from them. I believe that except for a positive blood culture and massive hemorrhage into the adrenal glands the autopsy showed little.

**A PHYSICIAN** Was the blood pressure taken in this case?

**DR. TRACY B. MALLORY** I think not. The history was very brief.

**DR. HAROLD L. HIGGINS** The commonest cause of embolic purpura is meningococcal septicemia ("spotted fever") with the purpuric spots elsewhere, as in the mucous membranes and in the organs. In this case one would expect the hemorrhages to have been in the adrenal glands. I should expect the blood pressure to have been very low. I recall one case with a systolic blood pressure of 40, and another with one of 50. Although this youngster had hemorrhages into the skin, there was no involvement of the meninges. I favor reporting the diagnosis as meningococcal septicemia with purpura and hemorrhage into the adrenal glands, rather than as the Waterhouse-Friederichsen syndrome. The former expresses the clinicopathological condition clearly; the latter calls for acquaintance with a clinical entity that is not so well known.

**DR. EDWARD F. BLAND** What is the source of the emboli?

**DR. HIGGINS** I look on meningococcal septicemia as being like anthrax. The organisms multiply so massively that they cause blocks of the capillaries. This blockage leads to extrusion of blood into the tissues and to the formation of

thrombi in the small veins, the latter being the source of the emboli. I should expect that this child had a massive meningococcal growth from the blood stream.

#### CLINICAL DIAGNOSIS

Waterhouse-Friederichsen syndrome.

#### DR. TEFFT'S DIAGNOSES

Waterhouse-Friederichsen syndrome, with massive hemorrhage into the adrenal glands.  
Probable meningococcal septicemia.

#### ANATOMICAL DIAGNOSES

Meningococcal septicemia.  
Hemorrhage into adrenal glands, bilateral.

#### PATHOLOGICAL DISCUSSION

**DR. MALLORY** The autopsy showed a tremendous number of scattered subcutaneous purpuric spots and massive hemorrhage into both adrenal glands. When one cut across them, the cut surface looked like smooth blood clot and one could not grossly recognize any adrenal tissue. The blood culture showed a growth of meningococcus. We have had so far as I know only one other case of this sort in the hospital from the blood of that case a gram-negative diplococcus was also grown. Although the organism was not an entirely typical meningococcus from the bacteriological point of view, I think there can be little doubt of its identity. I am willing to consider both Dr. Tefft and Dr. Higgins correct. The case certainly fits the Waterhouse-Friederichsen syndrome perfectly, and unquestionably the primary underlying trouble was a fulminating meningococcal septicemia. How often that may be the case, I am not aware. At the Children's Hospital I understand that all the cases have shown meningococcal septicemia.

**DR. TEFFT** In later years it has been reported in most of the cases where it has been searched for.

**DR. MALLORY** It would be a comparatively easy organism to miss. Therefore, I should not take negative reports very seriously unless some other pathogenic organisms, such as staphylococci and pneumococci, had been recovered.



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The Waterhouse-Friederichsen syndrome is

portant drugs, particularly those, such as quinine and morphine, that are obtained in their raw states from countries with which commerce, at present, is extremely restricted

Such plans for total war, together with the other necessary steps in medical preparedness, constitute a vast task for the medical profession. It is, however, one that can, and will, be met, with the aid of governmental agencies, public-health departments of states, cities and towns, the National Research Council and national voluntary organizations interested in health and disease. But in order to start the ball rolling, and rolling at the proper speed and in the right direction, the official appointment of a medical co-ordinator or of a co-ordinating board is of prime importance

### WILD LIFE UNCONTROLLED

EVEN early in September the abundance of insect life in New England is apparent. It is already probable that no large-scale poliomyelitis outbreak will occur this year, but the thought of this disease, which may have nothing whatever to do with insect life, is always a reminder of those things which evolve about us, perhaps within our midst, but not well within our control. Some of them are pests, some are menaces, some are merely nuisances. In the last century if the farmer wanted apples he just grew them but now he must protect his orchards against a variety of parasitic life. To what extent these pests are increasing or how much of their prevalence is due to increasing recognition is difficult to know. There is no doubt that both these changes are taking place, and that our expanding knowledge confronts us with an ever-mounting range of problems.

So far as disease in human beings is concerned, the control of the dog can practically control rabies. But in rural regions the control of the dog to say nothing of other minor domestic animals, is impossible. If a dog is going to be a dog or a cat a cat, it will hunt and forage in the country or suburban regions to the point that it will expose itself to those vast reservoirs of wild life for which we cannot provide anything which approaches regulation or even understanding. Skunks, squirrels

and snakes, birds, bats and bugs, ticks, toads and turtles, flies, fleas and fish, how near all of these may be!

The control of rats has in the past sufficed to control outbreaks of plague. The first outbreak in San Francisco, in 1900, and the recurrence after the earthquake and fire, in 1907, were both suppressed by systematic efforts to destroy rats and their harborages. The continuation of these efforts has reduced the cases of plague in this country to less than one a year for the past decade, and yet field studies reveal that there has been a gradual extension eastward from the Pacific Coast. From rats the disease infected ground squirrels and other wild rodents, and has now been associated with a wide variety of the wild life of the southwestern states. It is of course more closely associated with the communal habits of their fleas and ticks than with those of the species themselves. Who will undertake the control of the fleas and ticks of the squirrels, wood rats, field mice, prairie dogs and rabbits of the western United States?

The recent appearance of Rocky Mountain spotted fever in New England, as well as the recognition of endemic typhus in the middle southern states, and the demonstration that these things can be transmitted by the common varieties of ticks and fleas, with which some of our summer resorts abound, are interesting. The thrills so dramatically associated with far-off expeditions of a medical nature may yet be had in our own back yards.

### MEDICAL EPONYM

#### DERCUM'S DISEASE

Francis Xavier Dercum (1856-1931), while instructor in nervous diseases at the University of Pennsylvania published a case report entitled *A Subcutaneous Connective Tissue Dystrophy of the Arms and Back, Associated with Symptoms Resembling Myxoedema* in the *University Medical Magazine* (1:140-150, 1888). Four years later when he was clinical professor of diseases of the nervous system at Jefferson Medical College he published a report of "Three Cases of a Hitherto Unclassified Affection Resembling in Its Grosser Aspects Obesity, but Associated with Special Nerv

ous Symptoms—Adiposis Dolorosa” in the *American Journal of Medical Sciences* (N S 104 521–535, 1892) In this paper he gave his first account of the disease and coined the name by which it is now known, adiposis dolorosa

Evidently the disease is not simple obesity It would seem, then, that we have here to deal with a connective tissue dystrophy, a fatty metamorphosis of various stages of completeness, occurring in separate regions, or at best unevenly distributed and associated with symptoms suggestive of an irregular and fugitive irritation of nerve trunks—possibly a neuritis

Inasmuch as fatty swelling and pain are the two most prominent features of the disease, I propose for it the name *Adiposis Dolorosa*

R W B

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS  
AND GYNECOLOGY\*

RAYMOND S TITUS, M D, *Secretary*  
330 Dartmouth Street  
Boston

CESAREAN SECTION AND INFLUENZAL PNEUMONIA

Mrs M F, a twenty-five-year-old primipara at term, was seen at home on January 24, 1929, with a temperature of 102.2°F., a pulse of 100 and respirations of 30 There were very few definite findings in the chest, and a diagnosis of influenza was made

The family history was unimportant, as was the patient's past history Catamenia began at thirteen, were regular with a twenty-eight-day cycle and lasted five days without pain The last menstrual period began on April 18, 1928, making the expected date of confinement January 25 The prenatal course had been uneventful

About midnight on January 24 the membranes ruptured, and at 3 a m, mild labor started The patient was admitted to the hospital about 8 a m, at which time she was having moderate five-minute pains Rectal examination showed that the presenting part was high, there was no dilatation of the cervix Labor continued throughout the day At 6 p.m there was still no dilatation and the cervix was moderately thick The presenting part was not in the pelvis Abdominal examination disclosed a vertex presentation At 8 p m a low transverse cervical cesarean section was performed under spinal anesthesia The immediate operative result was good, and a living male child weighing 7 pounds, 15 ounces, was delivered At the close of the operation the mother's condition was fair

\*A series of selected case histories by members of the section will be published weekly Comments and questions by subscribers are solicited and will be discussed by members of the section.

The day following operation the patient's abdomen became distended and the respiratory infection was worse The temperature was 102°F., the pulse 120, and the respirations 28 A medical consultation was held, and a diagnosis of influenzal pneumonia was made The patient was placed on a pneumonia regime and digitalized The distention was treated with 1/150 gr eserine sulfate every four hours for four doses, flaxseed poultices and a rectal tube

In spite of the above treatment, the distention became worse and the cough increased On January 31, the sixth postoperative day, a small amount of pus was draining from the operative incision On the following day it was noted that the incision had separated and that a loop of intestine protruded A surgical consultation was held, and immediate repair advised The wound was resutured under spinal anesthesia

For ten days following this second operation the patient's temperature fluctuated between 104 and 100°F On February 9 the chest condition had cleared, and on February 12 the temperature dropped to normal, where it remained until discharge on March 4

*Comment* This patient was a very sick woman—labor, cesarean section, influenzal pneumonia, wound sepsis That she recovered speaks worlds of praise for the care which she received Spinal anesthesia was undoubtedly the ideal anesthetic for the cesarean section, which was necessary to ensure a live baby The unusual complication of sepsis of the wound with extrusion of a loop of bowel was attacked immediately, and fortunately the result was successful The patient owes much to the care she received

CORRESPONDENCE

PLANS FOR BUDGETING THE COSTS  
OF MEDICAL CARE

*To the Editor* This letter concerning group health services in Massachusetts is written in order to clarify a subject that may still be confused and to indicate some comparisons and suggestions that may lead to constructive thought and action I have learned of the confusion of thought concerning the White Cross Health Service through having had the privilege of several conferences with members of Medical and Surgical Associates and then finding among physicians opinions about the operation and purposes of this plan at variance with my own impression. Because this difference of opinion seems to me to rest principally on misunderstanding or lack of understanding and because considerable time has elapsed since information concerning the White Cross has appeared in the *Journal*, it may be in order to present the viewpoint of a practitioner not associated with the plan In order to avoid inaccuracies in dealing with this subject, the facts and purposes pertaining to the operation of the White Cross that appear in this letter have been set forth by one of the members of Medical and Surgical Associates.

The present interest in and growth of group health services are due primarily to recent advances in medical knowledge. These advances are largely responsible for the increased effectiveness of preventive medicine and medical therapy. The resulting decrease in mortality and morbidity rates has made the budgeting of health services rational. The medical profession, the public health service, the daily press, radio movies and last but not least, the personal experience of individuals have taught the public much about "modern medicine." But much health education remains for the future. Because of lack of an understanding of how to obtain medical care and budget a cost good medicine, as differentiated from poor medicine, is not being financed voluntarily by the public so adequately as it should be. Too much money is being wasted on quack remedies and cults. Too many people find that they are unable to pay the costs of good medical care when they are faced with the burdens of illness. Persons with family incomes as high as \$30 to \$40 per week are admitted to our hospitals as charity patients. The Senate Committee to consider the Wagner Health Bill concluded that, under existing medical practice, families with incomes as high as \$3000 or more per year are frequently unable to meet the costs of serious illness.

Several years ago the American Hospital Association encouraged the establishment of hospital service corporations to facilitate and increase the utilization of hospitals by the public. Most of these services have been carefully controlled and managed. They are enabling subscribers unfortunate enough to suffer serious illness to obtain good hospital care without excessive expense; they permit members in good health to enjoy for relatively little cost the knowledge that they too may receive such care when the need arises; they increase the subscribers' financial ability to pay for their professional medical care and finally they not only are augmenting the utilization of hospitals by paying patients, but also are obtaining voluntary financial support from large sections of the public.

Thus, the American Hospital Association has readjusted hospital service to the demands that advances in medicine place on it. The medical profession needs, likewise, to readjust medical practice to the advances in medical knowledge if it and the public are to profit by them. Practical common sense, not welfare sentimentality suggests some readjustment in order to finance good medicine, which today means expensive medicine and good doctors adequately remunerated.

During the past two years two steps have been taken in Massachusetts toward such adjustment of our medical services.

In April, 1939 the Massachusetts Medical Society recognized the desirability of providing an opportunity for the public to budget voluntarily the costs of professional medical care. During the course of the year the Society arrived at certain conclusions concerning a service which the Society itself proposes to establish and operate. These may be outlined as follows: first, that the necessity of a cash reserve to cover the liabilities of the service requires operation of the service as an insurance business under the laws and supervision of the Commonwealth pertaining to such business; second, that an enabling act should be obtained from the legislature; third, that this proposed service should grant to any subscriber the right to choose any physician for medical care.

While the Society was evolving these principles, a lay group, known as Health Service, Incorporated (White Cross) obtained a charter to establish a non profit health service. This service then entered into a contract with a medical partnership for the provision of medical care to White Cross members in the vicinity of Boston. The preliminary drafts of this contract and the agreement be-

tween the White Cross and its subscribing members were placed before the profession by publication in the *Journal*. Since then the White Cross has made it clear that this medical partnership is not to have a monopoly of the medical care under this health service. The White Cross desires, with the advice of an advisory council of physicians to enter into agreements with other groups of physicians for the provision of medical care to subscribing members in other communities.

Through these agreements with such groups of physicians, provision is made for the medical care of White Cross members to be entirely in the hands of qualified physicians. It is pointed out that contracts are made with recognized groups of physicians in order to have an administrative unit for the medical services of each geographical group of subscribers. Thus, the White Cross believes, is essential to efficient operation of the service. If a single medical group formed the only administrative unit, its administrative functions might become too large and the local needs and facilities might not be wisely met and utilized. The danger of these administrative groups of physicians arbitrarily restricting the physicians participating in the medical care is prevented by the freedom given members in choosing their physicians. Subscribing members may choose as their family physician or family pediatrician any physician who has graduated from a Grade A medical school is on the staff or courtesy staff of an approved hospital in the community in which he practices and agrees to be an associated physician of the group of physicians providing medical care to subscribing members. A White Cross member and his associated family physician may then call in any specialist or consultant who is qualified as such by a medical board of certification. Thus qualifications already established by the medical profession through existing medical societies define the eligibility of physicians. Judgment by administering physicians is avoided yet necessary provision is made for protecting the standards of efficient operation of the service. At the same time subscribers are given freedom of choice of physicians within the broad limitations of these qualifications.

Thus, it would seem that the service in a very conservative manner is built around the family practitioner. The personal relation between physician and patient is perhaps more protected than under existing private practice because continuity of the relation between doctor and patient will be encouraged. The family physician is coordinated with accredited specialists who are on the staffs of the well-equipped hospitals of the community. Thus, without disturbing the family physician or specialist in his private practice this service simply but rather admirably organizes and utilizes the medical knowledge and facilities of a given community.

The details of the Society's plan have not so far as I know been worked out. How long a time will be required before this can be done, before finances are provided, and before the plan is put into operation is still unknown. The White Cross operating on the simpler and less extensive basis has within the past nine months worked out the details and become in its small conservative way a going concern. It has been investigated by one of the foundations interested in matters pertaining to health and has received financial support from this foundation and from individual residents of Massachusetts. As the public becomes aware of the opportunity to subscribe to this service, which is organized to provide an excellent quality of medical care, the membership should increase. Provision is made for subscribing either as members of employed groups (as is done under the Blue Cross) or as individuals. A high percentage enrollment from a group should be required in order to secure a cross section of health. To

obtain desirable percentages, considerable contact must be provided between prospective subscribers and the White Cross. The details of the service will have to be described and discussed with the interested groups. This essential contact and discussion should be accomplished without transgressing professional ethics. In this connection, it is of interest to note the provisions for observing ethical conduct in accepting individual members. Individuals may become members under somewhat higher subscription rates and upon condition that their acceptance will be dependent on passing a physical examination and their obtaining a statement from any physician treating an existing ailment that payments and obligations have been satisfactorily discharged.

There seems little in the White Cross plan that is not conservative and does not meet the criteria of fair and desirable competition and ethical conduct.

In comparing the Society's projected plan and the White Cross service, the following differences are clearly apparent.

The former is an insurance service. It must, therefore, carry the legally required cash reserves. This complicates its structure and operation and may increase its operating costs. The latter is a health service whose obligation is a service and is, therefore, free from a cash liability that requires legal insurance reserves.

The Society's plan permits complete freedom of choice of physician and in so doing does not protect the average subscriber or average participating physician from the inefficiency and the costs of poor medicine. With about 2000 licensed physicians in the Commonwealth who are not members of the Massachusetts Medical Society and many of whom are graduates of medical schools that are disapproved of by the Society, the maintenance under the Society's free-choice plan of a quality of medicine that permits efficient operation will be difficult. The White Cross plan permits freedom of choice of physician by subscribers from among those physicians who meet certain qualifications already established by the medical profession. This limitation of choice protects both the subscriber and the participating physician. It is a conservative measure which should facilitate the successful operation of the service.

There seems to be little reason for conflict between these two services. The lessons learned by the one should be helpful to the other. Competition between the two is desirable and not dangerous to the profession as the medical service and standards under each are controlled by the profession. It is to the interest of physicians that both services succeed. The failure of either can result only in loss to the profession. For they are both an attempt to extend voluntarily supported medicine of a good quality.

The White Cross plan appears to be of particular interest as a conservative experiment in budgeted health service that lays particular emphasis on protecting the quality of medical care. Believing that it should be supported by the medical profession as an experiment from which much benefit to the public and the profession may be derived, I wish, in the hope of contributing to its success, to submit the following three suggestions.

That the White Cross establish a council of physicians to advise it concerning the selection of administrative groups of physicians in the various localities where there are subscribing members. The physicians comprising this council should be respected physicians who preferably are not members of any administrative group of physicians associated with the service.

That, as soon as practical, the members of administrative groups of physicians be physicians actively engaged in the practice of medicine. In this connection

there has been some criticism of the present personnel of Medical and Surgical Associates. It should be appreciated, however, that the initiative in starting the medical service under this plan could hardly have been undertaken by many practitioners. Now that the service is operating, the desirability of having it controlled by practitioners seems clear.

That the single-income limit of eligibility of subscribing members be modified to provide a shifting scale based on size and financial obligations of the family. In considering this limit, it must be recognized that this is a self-supporting service, that the membership dues must be adequate to provide fair remuneration of the participating physicians, and that, therefore, limits must not be set which will restrict membership to an income level in which individuals cannot afford the necessary subscription rates.

Provision of health services to those individuals who cannot afford such payments as will make a service self-supporting is a different matter. Since the provision of such health services will probably involve the use of tax funds, their consideration should be entirely separate from discussions pertaining to voluntary self-supporting services, such as the White Cross. Let us hope that such experiments as the White Cross or the Society's plan will enable us to cope successfully at a later time with this other problem.

WALTER P. BOWERS, M.D.

264 Chestnut Street,  
Clinton, Massachusetts

## NOTICES

### ANNOUNCEMENT

JAMES HARRISON, M.D., announces the removal of his office from 120 Needham Street, Dedham, to 57 Bridge Street, Dedham.

### NEW ENGLAND DERMATOLOGICAL SOCIETY

The next regular meeting of the New England Dermatological Society will be held at the Massachusetts General Hospital, Skin Out Patient Department, on Wednesday, October 9, at 2 00 p.m.

### SOCIETY MEETINGS AND CONFERENCES

- SEPTEMBER 12-MAY 8—Pentucket Association of Physicians Page 263 issue of August 15
- SEPTEMBER 16—New England Society of Anesthesiology Page 305 issue of August 22
- SEPTEMBER 16-20—American Occupational Therapy Association Page 263 issue of August 15
- SEPTEMBER 17-19—Clinical Congress of the Connecticut State Medical Society Page 305 issue of August 22
- SEPTEMBER 27-28—New England Surgical Society Poland Spring, Maine
- OCTOBER 6-11—Annual meeting of the American Academy of Ophthalmology and Otolaryngology Page 81 issue of July 11
- OCTOBER 8-11—American Public Health Association Page 655 issue of April 11
- OCTOBER 9—New England Dermatological Society Notice above.
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# The New England Journal of Medicine

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VOLUME 223

SEPTEMBER 12, 1940

NUMBER 11

## CARE OF THE BACK FOLLOWING SPINAL-CORD INJURIES\*

### A Consideration of Bed Sores

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BOSTON

LIKE Mark Twain's weather, everybody talks about the bed sores associated with spinal cord injuries but no one does anything about them. They are regarded as the natural accompaniment of these lesions. When a bed sore develops on a patient, the doctor in charge feels vaguely put upon, makes a variable number of futile therapeutic gestures and finally lets Nature take its course. If asked about the reasons for its development he speaks of "trophic effects" and "trophic nerves," ignoring the fact that he has not the slightest idea what either phrase means. It is my purpose to present herewith a tentative explanation of the bed-sore problem as it relates to spinal-cord injury together with the evidence on which the explanation is based and certain conclusions relative to the therapy of this annoying and serious condition.

Provided the skin is primarily undamaged, bed and pressure sores develop only because of secondary destruction of local tissue. That there are certain mechanical factors which will cause this destruction is familiar to everybody. That the latter are secondary rather than primary elements is not so well recognized, however. The occurrence and extent of this destruction depend on the presence of a bony weight-bearing prominence close beneath the skin, the thickness of the padding tissue between the bone and the skin itself, the length of time that constant weight-bearing is permitted over this point and the integrity of the protective horny layer of the skin. The first two and the last of these four factors obviously determine the usual sites at which bed sores develop. Thus, the sacrum, the trochanters, the calcanei at the insertion of the tendo Achilles, — not the heel proper, — the angles of the scapulae,

the occiput and the like are usual regions where such sores may develop in a bed ridden patient, especially if for any reason he is cachectic. The third factor is largely dependent on the presence of a local anesthetic area, and therefore becomes an integral part of the spinal-cord phase of the problem. Under ordinary circumstances, no one of these conditions causes destruction of tissue. There must be in addition a local anoxia and anemia.

A knowledge of the conditions that produce such anoxia is indispensable. It requires, moreover, an understanding of the anatomy and physiology of the cutaneous blood supply. The Suttons<sup>1</sup> give an excellent description of the anatomy involved. They state that the skin is supplied with blood through two horizontal plexuses. The arteries come from beneath and are largest in the regions exposed to pressure (volar, gluteal). They anastomose deep in the corium to form the arterial rete. From this, branches run to the upper third of the corium to form a second plexus, which is a sub-papillary network. Arterioles, certain of which anastomose with the veins beneath by way of the Sucquet-Hoyer canals, arise from this network to supply the papillary layer, hair follicles and sebaceous glands, they are end arteries. Capillaries from the arterioles enter the papillae and form beds. The walls of these capillaries have tonus because of the presence of the cells of Rouget. The normal blood pressure of skin capillaries approximates 20 to 40 mm of mercury but the walls can withstand an expanding pressure of 100 mm. The normal pressure rises to 35 to 45 mm in reactive hyperemia and to 70 to 80 mm in response to the local application of heat. The epidermis has no blood supply. Anatomically, then it is apparent that the papillae lying immediately below the avascular epidermis, contain contractile capillaries arising from arterioles

\*Read in part before the joint meeting of the Philadelphia Academy of Surgery and the Boston Surgical Society Incorporated, on March 4, 1940, at the Boston City Hospital, Boston.

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which in their turn are the end vessels of two deeper plexuses. There is a possible direct communication between the arterioles and the veins. The veins otherwise approximate the arrangement of the arteries and are also contractile.

Much of the physiology of the blood supply to the skin, especially in parts other than the extremities, is still either controversial or unknown. The mass of conflicting and confusing literature has been reviewed and oriented up to 1939 by McDowall<sup>2</sup> in his volume, *The Control of the Circulation of the Blood*, which supplements the earlier and more limited work of Kuntz.<sup>3</sup> I quote from both references freely. Certain tests have been shown to produce constant reactions. For example, stroking and local compression of the skin, under normal conditions, produce first an area of pallor, which is due to a localized constriction of the capillaries. The reaction takes place in regions in which nerves have degenerated or have been anesthetized as well as in regions with the nerve supply intact. After a definite interval and after the pressure has been removed, the pallor is ordinarily succeeded by an irregular-shaped blush or flare. The flare depends for its presence on the integrity of the peripheral nerve supply to the injured area and is due to arteriolar dilatation. A more prolonged pressure produces local tissue asphyxia which may have wheals or blisters associated with it. This is known as reactive hyperemia, and is a type of vasodilatation produced by the presence of an abnormal amount of local metabolic substances. It follows only such stoppage of the local circulation as causes tissue damage. In addition, prolonged pressure on the skin causes first pain and then local anesthesia. It is this local reaction that produces pressure sores as distinct from bed sores. As will be seen, the latter develop when associated with a spinal-cord injury, after certain other changes have been added to this fundamental reaction.

Except for this purely local mechanism, which as noted above is dependent on the integrity of the regional nerve supply, the physiological control of the cutaneous blood supply is believed to rest in the main on reflexes that are mediated by way of the sympathetic and parasympathetic nervous systems. The sympathetic pathways are well known so far as the skin is concerned, the impulses that pass over them being exclusively vasoconstrictor in type. The reflex arc lies entirely below the level of the sensory thalamus,<sup>4</sup> and can be shortened sufficiently to be limited to the spinal cord. The parasympathetic pathways for impulses to the vessels in the skin are unknown. There is some evidence that the latter leave the spinal cord by

way of the posterior spinal roots and reach the cutaneous vessels by way of the peripheral mixed nerves. In all probability, this parasympathetic reflex arc can also lie within the limits of the spinal cord, but its connections are not certainly known. The impulses are vasodilator in type. Normally, according to Bozler,<sup>5</sup> it may be assumed that stimulation of the dorsal spinal roots produces a vasodilator substance at the nerve endings and stimulation of the sympathetic system a vasoconstrictor substance. If these two substances are not in balance and mutually neutralized, either vasoconstriction or vasodilatation will follow.

Thus it may safely be said that under normal conditions an adequate supply of blood to the skin depends on the integrity of two reflex arcs, which must include at least the spinal cord. One

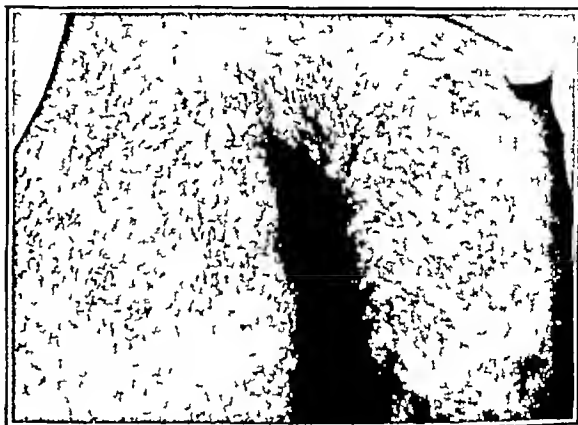


FIGURE 1 *Hyperemia over the Sacral Region*  
In this patient, who had a cervical cord injury, part of the hyperemic area necrosed later to become a pressure sore.

of these—the sympathetic—is well understood and has central connections in man in at least the thoracic and upper lumbar cord. The pathways of the other are not well known but probably include the dorsal spinal roots. Proper response on the part of the cutaneous circulation to varying local needs requires instant correlation between these two reflex mechanisms. Failure on the part of either necessarily impairs the vitality of the cutaneous tissue that their interactivity is designed to protect. In addition, local injury to the skin produces strictly local changes in the blood supply. These are in the nature of a reactive hyperemia, which may be associated with tissue asphyxia but which does occur independently of the central reflex connections. Failure of the reflex control of the cutaneous circulation, when added to the local changes that have produced or will produce a pressure sore, causes a bed sore to develop on this site.

Whether or not the spinal cord is involved one may assume that any of the usual conditions is able to produce a pressure sore. Such a sore is generally noted first as a localized area of redness (Fig 1). The epidermis then disappears, either by way of a blister or on the dressing without any other noticeable preliminary and the reddened area is changed into a weeping surface in which the papillae are clearly visible (Fig 2). Further progress usually depends on the effects of local infection. If, however, the ulcer is kept sterile, and the causative factor is allowed to persist, deeper necrosis associated with serous discharge and further marked hyperemia follows, after which local infection is inevitable. With the onset of infection, the ulcer becomes a classic septic, granulating wound containing varying amounts of necrotic tissue (Figs 3 and 4). Its

well as their lack of knowledge as to how to assure it. Such pressure sores develop despite the normal activity of the sympathetic and parasympathetic reflexes. The first stage, which is ordinarily



FIGURE 2. Necrosis and Loss of Epidermis  
Note the prominent papillae and the appearance of exuding serum on the surface

progress depends on the adequacy of the surgical care. One characteristic stands out, however. Except in patients with extreme cachexia or in the presence of unreasonably prolonged immobility the pressure sore has little or no tendency to spread radially and if it does so the reason can always be found in the inadequacy of the surgical treatment or in the failure to correct the underlying causative factor. Common examples of the latter are the unwillingness of the surgeon to remove a cast that is causing local pressure, and of the former the ignorance on the part of all attendants of the indispensability of a constantly dry bed as

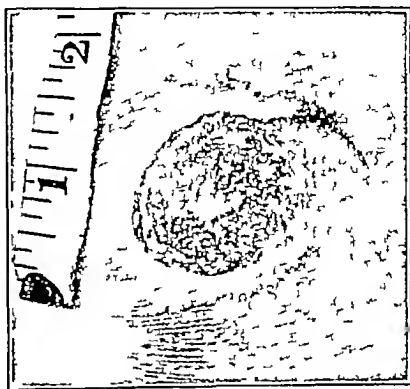


FIGURE 3. A Pressure Sore with Necrosis  
This had failed to enlarge after being present for nine months. The patient had a transection of the cervical cord

not seen, is pallor of the skin from local anemia. This is followed by the characteristic flare. It exemplifies the classic reactive hyperemia, with

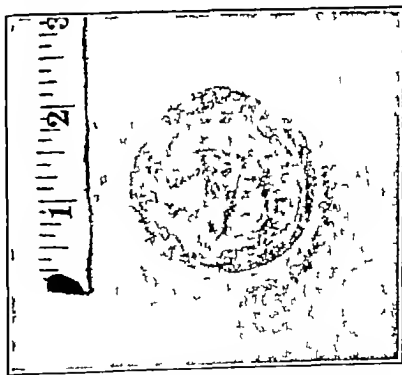


FIGURE 4. A Pressure Sore with Local Infection  
This was the same age and on the same patient as the one illustrated in Figure 3. The location was different however

local tissue asphyxia and all the accompanying chemical and cytologic changes. Such pressure sores can be caused by any of the mechanical factors noted above.



On the other hand, bed sores that develop in association with spinal-cord injuries are different from pressure sores. They start earlier in the course of the disease, spread radially almost at



FIGURE 5 A Typical Bed Sore

Note the tendency to radial spreading. This patient had a transection of the thoracic cord. At the time the bed sore was photographed, it had been present for six months.

once (Fig 5), and continue to do so for long periods. They may resume their lethal spread at any time after it has been stopped if the patient becomes exhausted or develops any significant infectious process. All this is in addition to the

bladder, the mechanism of which is now well established.<sup>9</sup> Reasoning from this analogy as well as from theoretical grounds, backed by such knowledge of the vasomotor reflexes as is possessed, bed sores should be especially common in thoracic-cord and upper-lumbar-cord lesions, that is, with the bone injury between the first dorsal and the first lumbar vertebra. It is here that the central connections of the sympathetic nervous system are made. As will be seen my experience bears out this theory.

During the ten years that the Neurosurgical Service has been established at the Boston City Hospital, 126 patients with spinal-cord injuries have passed through my hands. Thirty (24 per cent) developed bed sores.

There were 26 patients with thoracolumbar-cord injuries, none of whom died within the first twenty-four hours after injury, and of these only 14 (54 per cent) developed bed sores, although all may be considered to have been eligible (Table 1). The sores were all primarily sacral in location. One developed following the application of a plaster cast sixty-nine days after injury; another six months after injury, after the patient had been allowed to lie in a wet bed for the first time. Two patients were admitted with large sacral sores already present, both were said to have appeared immediately after the accidents (shootings), which occurred thirty-one days and two years previously. Of the remaining 10 patients, 1 is known to have had a bed sore develop in two hours after injury, 1 in twenty-four hours, 1 in three days, 1 in four days, 1 in five days, 3 in

TABLE 1 Data on Cases with Thoracolumbar-Cord Injuries

LOCATION OF LESION	NO OF CASES	CASES WITH BED SORES %	HOSPITAL DEATHS		HOSPITAL MORTALITY %	DEATHS AFTER DISCHARGE	TOTAL MORTALITY %	NO OF CASES AT HOME OR AT HOSPITAL	NO OF CASES LOST
			WITHIN 24 HRS.	TOTAL					
Thoracolumbar cord									
All cases	26		0	17	65	3	77	6	0
Those with bed sores	14	54	0	10	71	2	86	2	0

reactive hyperemia and local anoxia of the underlying pressure sore.

Based on our knowledge of the deleterious effect of spinal shock on all reflex activity below the level of any spinal-cord injury, its presence immediately after the injury and its characteristic continuation or recurrence whenever exhaustion or sepsis develops, I have assumed that the difference between the ordinary pressure sore and the bed sore associated with any injury to the spinal cord exists because of the influence of spinal shock on the peripheral vasomotor reflexes. An analogy is found in the effects of spinal shock on the

six days, 1 in seven days and 1 in eleven days after the accident. Nine of the 14 patients had transected cords and the other 5 suffered from contusion with a physiologic transection. One patient is still in the hospital, 1 is leading a satisfactory wheel-chair life at home five years after injury, 1 died of pneumonia at another public institution three and a half years after injury, and 1 died six weeks after returning home in a hopeless condition. The other 10 patients (71 per cent) all died in the hospital, but I am not certain as to the cause of death. I had believed it was sepsis, but recent experience leads me to ascribe the

deaths to more fundamental changes in the body chemistry. In support of this theory there was a marked drop in the serum protein levels in the cases with significant bed sores but no conclusions are justifiable as to the significance of this observation. Furthermore, this drop seemed to be commensurate with the diameter and depth of the ulcerated areas.

Seventy-six of the cord injuries were cervical (Table 2). Ten patients died within twenty-four

seven years in another public institution. The other four were self-supporting and well two, two, four, and an unknown number of years after the injury, respectively.

Twenty-four patients had injuries of the cauda equina (Table 2). None died within twenty-four hours of the injury, so that all were eligible for bed sores. Three patients (12 per cent) developed bed sores. One sore was in the sacral region, and developed thirteen days after a laminectomy ac-

TABLE 2 Data on Cases with Cervical-Cord and Cauda Equina Lesions

LOCATION OF LESION	NO. OF CASES	CASES WITH BED SORES	HOSPITAL DEATHS WITHIN 24 HRS.	DEATHS TOTAL	HOSPITAL MORTALITY %	DEATHS AFTER DISCHARGE	TOTAL MORTALITY %	NO. OF CASES AT HOME OR IN HOSPITAL	NO. OF CASES LOST
Cervical cord									
All cases	76		10	36	47	4	53	32	4
Those with bed sores	13	20*	0	7	54	1	61	5	0
Cauda equina									
All cases	24		0	2	8	0	8	18	4
Those with bed sores	3	12	0	1	33	0	33	4	1
Cervical cord and cauda equina									
All cases	100		10	38	38	4	42	50	8
Those with bed sores	16	18	0	8	50	1	56	6	1

\* Exclusive of patients who died in the hospital within twenty-four hours.

hours after their injury and must therefore be discarded as not eligible for bed sores. Of the remaining 66 patients 13 (or 20 per cent) developed bed sores. One had a sore on the occiput because of improper traction twenty-five days after the accident, 2 developed sacral sores nine and twenty-four days respectively after the accident and immediately following the application of plaster jackets, and 1 developed a sacral sore eighty-three days following the accident after being allowed to lie in a wet bed for the first time. Of the remaining 9 patients, 1 had pressure sores rather than bed sores but is included in the series nevertheless. He is still in the hospital and has a transverse myelitis from a thrombosis which followed cervical hematomyelia and edema (Figs. 3 and 4). Two of his sores are trochanteric and developed at the site of abrasions twenty-four hours after the accident. So far as the rest of these patients are concerned, the time of onset of 1 bed sore is unknown, 1 developed in one day, and 1 each within two, seven, nine, ten, fifteen and sixteen days following the injury. Seven or a little more than half of the cervical patients with bed sores died in the hospital. Two had transections, 2 had contusions, and the other 3 had hematomyelia. The cause of death was sepsis from an undrained perineural abscess in 1 case, pulmonary embolus from a femoral phlebitis in 1 and was undetermined in the 5 others. All the 5 patients who left the hospital alive had hematomyelia. One of them died of cancer of the rectum after

complicated by a considerable manipulation of the cauda. The operation was performed thirteen years after the injury. Another was in the lower thoracic region, and followed rapid hyperextension and the application of a plaster cast sixty days after the accident. The third sore occurred on the buttocks at the site of abrasions sustained at the time of the accident, it was present on admission. This patient died one month after admission from septicemia caused by an infected operative wound. Of the other 2 patients, one was well ten years after discharge and the other has been lost sight of.

Thus it will be seen that 54 per cent of the patients with thoracolumbar-cord injuries developed bed sores. The severity of the injury and of its complications is indicated by a group hospital mortality of 71 per cent. To be sure, practically all these patients had anatomic or physiologic transections, but this cannot be held to be the determining factor in the production of the bed sores, since such sores have developed also in association with other types of cord injury. However it unquestionably plays a part. In contrast only 18 per cent of the patients with injuries of the cervical cord and cauda equina had such bed sores. The hospital mortality of this group was only 50 per cent. These discrepancies are too great to be either coincidental or due to factors other than that of the location of the cord injury.

Of the other factors that might influence the occurrence of bed sores the only important one

is the variation in the treatment of the cord injury as applied to the different sites of cord damage. Within the limits of the individual characteristics inherent in the injuries themselves, all, at no matter what level, have received identical treatment. At the time of admission, any surgical shock that may be present is dealt with first. Simultaneously, the patient is put on tidal drainage.<sup>6</sup> After the surgical shock has been cared for, a cystometrogram<sup>7</sup> is made and the height of the siphon curve on the tidal drainage apparatus is adjusted accordingly. A lumbar puncture is next done, and the presence or absence of a spinal sub-

hospital mattress, with the bed made up in the ordinary way. Forcible rapid extension, Bradford frames, plaster-of-Paris jackets, rubber or other types of rings, lamb's wool pads and the like are not only no longer used, but are considered to be contraindicated and to be prolific sources of bed sores. The patients are kept scrupulously dry and are turned on an hourly schedule, their backs being rubbed, dried and powdered at each turning. It is interesting that profuse sweating has had no deleterious effect on the skin.

If the early signs of the presence of a pressure sore appear, the hyperemic areas are painted with



FIGURE 6 *Hyperextension of the Thoracic Spine by Means of a Blanket Roll and Bedboards*

arachnoid block is determined. If there is a block and the lesion is thoracic, a decompressive laminectomy is performed unless a major dislocation is present. If it is, the laminectomy is deferred until after a moderate degree of hyperextension of the spine has been attained, by placing opposite the kyphos an increasingly enlarged roll of blankets between the mattress and bedboards which rest on the springs (Fig. 6). If the block is decreasing after forty-eight hours of this therapy, operation is usually unnecessary. Cervical cord injuries that have a cerebrospinal-fluid block are not operated on for at least five to seven days.<sup>8</sup> Injuries about the crura, if acute, are treated by frequent lumbar drainage, which is continued until the fluid is free of blood. The late ones are explored. All patients are kept on the regular

tincture of benzoin twice in twenty-four hours. If the pressure sore develops into a bed sore or if the tissue destruction is merely the local type that goes with a pressure sore, the skin edge around the ulcers is treated in the same way. Sloughs and gangrenous tissue are never cut off but are allowed to stay in place until they fall off. Abscesses are tapped and emptied through the needle. Incision and drainage is contraindicated. Attempts to isolate the infecting organism have nearly always been unsuccessful on account of the large number of contaminants. However, ulcerated areas that are infected with *Streptococcus hemolyticus*, as determined by culture, are dressed with gauze saturated in a solution of sulfanilamide. Zinc peroxide as advised by Meleney and Harvey<sup>9</sup> should be used if the infection can be shown to be a micro-

aerophilic hemolytic streptococcus. No such case was recognized in this series. Other ulcerated surfaces are wiped clean twice in twenty-four hours. No local application is used. High vitamin and laterly high protein diets, transfusions as indicated, adequate fluids, appropriate chemical treatment of the bacteriuria that is always present and physiotherapy are adjunct measures. In the past, I have tried and discarded all the ordinary forms of local applications, including tannic acid, gentian violet, scarlet red, Eozymol and so forth, strapping of the ulcer as recommended by Carty<sup>16</sup> all types of ring supports under back and heels, Bradford frames, sawdust beds and lambs wool pads. The same may be said of all types of mattresses except the modern, sponge-rubber one, which promises to be helpful.

My experience thus indicates that the only therapeutic essentials to prevent the development of bed sores are to move these patients on an exact hourly time schedule, to avoid, except as described above, all forms of external artificial splinting or support to the spinal column so long as the patient is bedridden, to prevent the development of any serious sepsis or exhaustion, and to keep the patient constantly and completely dry—a desideratum that can be accomplished only by the use of a properly adjusted tidal-drainage apparatus. Tincture of benzoin is the only worthwhile local application, and sponge-rubber mattresses appear to be desirable and useful in thoracic-cord injuries. Active surgery and wet dressings are contra-indicated.

#### DISCUSSION

The occurrence of both bed and pressure sores should be explainable by one fundamental process. This process should be based, if possible, on known facts, and should eliminate such highly theoretical concepts as are suggested by the unexplainable terms "trophic nerves" and "trophic changes." Although some gaps remain to be filled in, it will suffice for the present to ascribe both types of lesions to a local tissue necrosis which is caused by a local impairment of the circulation. The therapeutic importance of this concept is obvious.

The application of the well understood experimental changes which, in a mild form produce local anemia and the hyperemic flare, to the more advanced clinical condition recognized as a pressure sore and accompanied by a variable degree of such local necrosis, seems well supported by known facts. That this is the first stage of the more complicated bed sore characteristic of spinal-cord injuries appears equally reasonable. Experimental evidence and certain physiological and clinical data in support of the latter contention have,

however, been lacking. The demonstration here with presented of the preponderance and greater seriousness of bed sores associated with thoracic as contrasted with all other cord injuries provides a great deal of the missing clinical proof. This is particularly true when the importance of the reflex control of the cutaneous circulation and of its intimate association with the thoracic cord by way of the central connections of the sympathetic nervous system is appreciated. If the immediate effect of the presence of spinal shock on this as well as all other reflex activities below the level of a cord injury, and its characteristic later recurrence in the presence of a serious infection or exhaustion are added to the process, while not proved in detail, is so clear as to supersede any other more theoretical explanation.

From a practical point of view, such an explanation is of great significance. To be sure, without further evidence it can apply only to the bed and pressure sores that develop in association with spinal-cord injuries or other processes—such as an operation—known to produce spinal shock. Furthermore care must be taken not to confuse the causative factors outlined in detail in this paper with the conditions, such as infection and the like, that do not cause but rather prolong the life of bed and pressure sores after they have developed. This situation has barely been touched on. If this explanation is accepted and properly applied it commits the surgeon to a form of preventive therapy that is primarily concerned with conserving and improving the local circulation. His attention must therefore be focused on those procedures that eliminate, so far as possible, prolonged local weight-bearing or irritation that prevent all maceration of the skin and the development of any major systemic infectious process and that otherwise tend to eliminate spinal shock or prevent its recurrence. Locally he will avoid such applications and surgery as are in the least degree destructive. He will recognize also that although bed sores may be associated with any level of injury to the spinal cord and cauda equina, they are three times as common and one and a half times as fatal in thoracic-cord injuries as they are in other spinal-cord injuries. He should therefore be more than usually careful in such cases to bear in mind the need for conserving their cutaneous circulation.

#### SUMMARY AND CONCLUSIONS

An explanation of the occurrence of pressure sores is offered. This is based on the presence of the well recognized experimental cutaneous hyperemic flare.

The occurrence of bed sores in association with spinal-cord injuries is explained on the theory that all bed sores start as pressure sores, but develop more viciously and more widely because of the deleterious effect of spinal shock on the local cutaneous vascular reflexes

Clinical evidence in support of these explanations is offered by virtue of an analysis of 126 cases of spinal-cord and cauda equina injuries, in which 30 (24 per cent) of the patients developed bed sores

Bed sores occurred in 54 per cent of 26 thoracolumbar-cord injuries The hospital mortality in this group was 71 per cent

Bed sores occurred in 18 per cent of the cervical-cord and cauda-equina injuries The hospital mortality in this group was 50 per cent.

On the basis of the fundamental conception that bed sores are specialized and more virulent forms of pressure sores which are associated with spinal-cord injuries, and which are themselves merely evidences of a local cutaneous circulation that has failed to the point of producing local tissue necrosis, therapy designed to conserve and prevent further interference with the cutaneous blood supply is recommended

The essentials of this treatment are as follows to move such patients—and particularly those with thoracic-cord injuries—on an hourly time schedule, to prevent the development of any serious exhaustion by appropriate feeding, transfusions, administration of vitamins and the like, to prevent the occurrence of sepsis and to maintain a constantly dry bed by the proper use of a tidal-drainage apparatus, and to avoid all forms of external artificial splinting or support to the spinal column so long as the patient with a spinal-cord injury is bedridden

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TUBERCULOSILICOSIS\*

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THIS paper reports the observations made in the serial examination of 207 employees in the granite industry who had silicosis complicated by pulmonary tuberculosis, and who were working on full or part time when originally examined

PATHOGENESIS

Tuberculosilicosis can be defined as the condition in the lungs caused by the combined action of tubercle bacilli and silica dust It differs from tuberculosis in a non-silicotic individual in that the disease process is not due to the tubercle bacillus alone The silica appears to impair the lymphatic drainage of the lung Linear and nodular fibrosis results, with frequent obliteration of the pulmonary capillaries In pneumoconiosis caused by non-siliceous dusts, linear and focal pigmen-

tations are produced as in chronic infections and arteriosclerosis, but the discrete nodulation is not present as in silicosis In silicosis the resulting local cellular proliferation consists primarily of nodules about 2 to 5 mm in diameter, composed of concentric layers of fibrous tissue, which are quite similar to those formed by tubercle bacilli<sup>1</sup>

It has been shown clinically, pathologically and experimentally that this characteristic fibrosis of the lung produced by silica predisposes the patient to tuberculosis Inorganic dusts, including silicates, with the possible exception of asbestos, do not generally result in such fibrosis unless mixed with some amount of free silica

The fibrous nodule is the characteristic lesion of silicosis, but a differential diagnosis between silicosis and tuberculosilicosis is one of degree There are no standards for a definite opinion in the borderline cases It is stated<sup>2</sup> that the amount and distribution of the collagen in the tissue reaction may help in differentiation One notes that

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in the presence of active tuberculosis the characteristic silicotic nodules are no longer clear-cut and sharply defined, the borders become irregular, and as the disease process advances the localized dense massive areas show ill-defined radiating borders.

Silicotic nodules may be present in the early stage of the disease and the x ray examination may yet be negative. Tuberculous infection may rapidly accentuate the nodules. In cases of silicosis preceded by short exposures to high concentrations of silica and followed by early death microscopic sections from autopsy material have shown many silicotic lesions not revealed by the x ray examination. Almost all these cases have a very acute tuberculous process.<sup>7</sup>

All observations appear to point to free silica as the substance that increases the liability to tuberculous infection. The silica is believed to act as a chemical irritant of pulmonary tissue and to be associated with the solution of the quartz found in granite. The rate of reaction is probably proportional to the size of the particles.<sup>4</sup> Only free silica seems to have any specific action on tubercle bacilli in tissue.<sup>8</sup> At the present time most of the evidence points to a decrease in tissue resistance to tubercle bacilli among patients with silicosis. Silica appears to enhance the growth of tubercle bacilli,<sup>4</sup> and there is ample evidence to show that tubercle bacilli grow rapidly in the presence of silicotic lesions,<sup>7</sup> but there is no proof that tubercle bacilli obtained from patients with tuberculosilicosis show an increased growth.<sup>8</sup>

It is possible that the non-siliceous components of granite dust reduce the effect of the free silica in quartz dust.<sup>9</sup> Clinical observations have shown that long exposures to granite dust are necessary to produce nodulation in men with no reinfection tuberculosis. There seems to be some protection against silica dust in the granite mixture, either by reduction of the total amount of inhaled quartz or by the chemical inhibition of the reaction of the silica in the body. Injection of granite dust into experimental animals has not caused so much reaction as has the same amount of quartz alone in the dust. Inhalation experiments have shown the same results.<sup>6</sup>

Inhalation appears to be the most frequent mode of entry of the tubercle bacilli in primary and exogenous reinfection tuberculosilicosis. Moist sputum droplets, infected dry dust and contact are the commonest methods of cross infection.

Ever since Collis pointed out the high incidence and chronicity of tuberculous infection in silicotic patients, experience has shown that many

cases of tuberculosilicosis are found if such patients are followed long enough. A quiescent, encapsulated tuberculous focus may be spread by the transportation of silica to the diseased area. The organisms may live for a long time in the silicotic mass without appearing to multiply there.

#### OCCUPATIONAL AND ENVIRONMENTAL FACTORS

The diagnosis of tuberculosilicosis requires, first, that the existence of a silicosis hazard shall have been proved. The occupational history and a study of the patient's environment must show the presence of dangerous concentrations of free silica in the breathing air level. This danger limit in the granite industry is usually set at 10,000,000 particles per cubic foot of air.

Petrographic analyses of granite samples from the Barre Vermont district have shown a content of 31 to 38 per cent of silica.<sup>1</sup> Average dust counts in the granite-cutting trade have ranged from approximately 60,000,000 particles per cubic foot of air for hand-pneumatic tool operators to less than 10,000,000 particles for attendant laborers.<sup>12</sup> The proof of silicosis usually requires an estimate of the time spent by the workman in the dust. In granite-cutting since the exposure is quite constant the history of the duration of the time spent in the industry is sufficient. On the other hand, the granite-quarrier whose work is more seasonal requires a more detailed occupational study. These men have been exposed to dust counts ranging from approximately 150,000,000 particles per cubic foot of air for the leyner drillers to 40,000,000 for the plug drillers.<sup>12</sup> It has also been shown that the dangerous particles are between 0.5 and 10 microns in diameter. In granite-cutting, 94 per cent of the dust particles have been found to measure less than 3 microns.<sup>14</sup>

Another contribution toward the diagnosis of tuberculosilicosis is the finding of a high local rate of pulmonary tuberculosis in any industry and its environment. From 1915 to 1936 the rate of actual to expected deaths from pulmonary tuberculosis among granite and sandstone stone cutters rose from 976 to 2693 per cent in other words the actual deaths were twenty six times those expected.<sup>16</sup>

The tuberculosis death rate has tended to remain high in Washington County the center of the granite industry in Vermont averaging 154 per 100,000 population per year for the period 1934-1937. The mortality for the rest of the state averaged 34 per 100,000 per year during the same period or about one fifth of that of Washington County.<sup>16</sup>

SYMPTOMS AND SIGNS

The onset of tuberculous infection in silicotic patients may be accompanied by no symptoms, by a general indisposition or by an explosive widespread dissemination of the disease process. The commonest symptom is dyspnea. This term is

TABLE 1 *Percentage Distribution of Symptoms, by Years of Service*

LENGTH OF SERVICE IN GRANITE INDUSTRY	DYSPNEA	COUGH	SYSTEMIC SYMPTOMS
yr	%	%	%
0-10	40	20	0
10-20	44	52	32
20-30	62	64	26
30 and over	83	65	10

generally reserved for the unusual breathlessness of which the patient complains following the exertion he undergoes at his regular occupation. He becomes conscious of a breathing effort that he had not noticed previously. In uncomplicated silicosis there may be a slight shortness of breath, with dyspnea and cough present later. As the tuberculous infection sets in the dyspnea usually increases, and appears altogether out of proportion to the amount of diseased area present.<sup>18</sup> The number of granite workers with tu-

TABLE 2 *Percentage Distribution of Symptoms, by Age Groups*

AGE	DYSPNEA	COUGH	SYSTEMIC SYMPTOMS
yr	%	%	%
20-30	0	0	100
30-40	30	30	12
40-50	66	78	37
50-60	62	51	16
60 and over	75	75	17

berculosilicosis who show definite dyspnea appears to increase with the years of service in the industry (Table 1).

This shortness of breath is frequently very difficult to differentiate clinically from that caused by chronic pneumonitis with bronchiectasis, bronchial asthma, pulmonary fibrosis with emphysema, carcinoma of the lung and cardiovascular disease due to arteriosclerosis, hypertension or syphilis. Cough, expectoration, chest pain and hemoptysis often accompany the onset of tuberculous infection in silicosis. As in pulmonary tuberculosis without silicosis, there may be systemic symptoms of toxemia consisting of weight loss, fatigue, weakness, dyspepsia, morning nausea and vomiting, nervousness, night sweats and fever. These seem to appear most frequently in granite workers at about the age of forty-five (Table 2).

The physical examination in cases of tuberculo-

silicosis is extremely variable. Most cases with early infection are free of physical signs. With consolidation and fibrosis present and predominant, there may be found diminished expansion, impaired resonance, diminished breath sounds and rales. Sibilant rales may be the only signs of conglomerate fibrotic areas. Cavities may result in bronchial or amphoric breathing. The correlation of the symptoms and signs through the medium of the physical examination frequently determines the degree of disability of the worker.

ROENTGENOLOGICAL FINDINGS

Bilateral nodular shadows in the chest x-ray films of granite workers are usually due to simple silicosis. However, it is difficult through the medium of a single film to differentiate early uncomplicated silicosis and tuberculosis. Silicotic

TABLE 3 *Results of Direct Smear Examinations of Sputum*

AGE	NO OF CASES	NO OF PATIENTS PERMITTING SPUTUM EXAMINATION	PERCENTAGE OF CASES WITH TUBERCLE BACILLI IN SPUTUM
yr			%
20-30	1	1	100
30-40	17	7	43
40-50	55	16	69
50-60	82	21	76
60 and over	52	15	33

nodules are frequently seen first as discrete nodular areas in the midportion of the lung fields. Their coalescence is represented by massive shadows. In uncomplicated silicosis the hilar shadows often recede even though the lung fields show more intense nodulation. Tuberculous infection is often noted in those cases in which the hilar shadows enlarge and become sharply defined. The onset of tuberculous infection is also noted in chests showing the appearance of hazy infraclavicular areas on one side during an inter-

TABLE 4 *Relation Between X-ray Evidence of Cavitation and the Finding of Tubercle Bacilli by Direct Smear in the Sputum*

X-RAY DIAGNOSIS	NO OF CASES	PERCENTAGE OF PATIENTS PERMITTING SPUTUM EXAMINATION	PERCENTAGE OF CASES WITH POSITIVE SPUTUMS
		%	%
Silicosis with infection and cavitation	118	40	71
Silicosis with infection and no cavitation	89	13	25

val of a few months. The nodular shadows present in previous films now rapidly grow irregular in shape and distribution.

In tuberculosilicosis the linear apical shadows

... to ... a ... for ... have ... of pulmonary tuberculosis ... These ... in the ... with ... is ... in ... For one ...

... a ... the ... of ... for ... the ... of ... the ... of ... the ... of ...



FIGURE 1

X-ray photograph of the chest of a hand pneumatic-tool operator in granite for seventeen years showing bilateral discrete nodular shadows with well-defined borders and localized density in the right upper lobe

This man was forty five years old and had no symptoms or signs at the time of the original examination. Serial examinations during a five year period have shown no change.

This case is one of silicons with inactive tuberculosis

but the conglomerate nodular are is persist unchanged for several years, whereas with infection present the edges of the nodules become fluffy and ill-defined

#### LABORATORY FINDINGS

The only absolute clinical proof of tuberculosis is the discovery of tubercle bacilli in the sputum. Direct smears usually detect tubercle bacilli only

a high percentage of positive sputums in forty to sixty year-old patients with tuberculosis (Table 3)

There appears to be a high correlation between the x ray findings of cavities in tuberculosis and tubercle bacilli in the sputum (Table 4)

The sedimentation rate is of some prognostic value when used serially. Not infrequently notes normal sedimentation rates in cases



culosilicosis that are progressive and have positive sputums

A negative tuberculin test aids in the rare case as a differential guide

CLINICAL FORMS

The clinical types of tuberculosilicosis are often similar to those seen in pulmonary tuberculosis

bercle bacilli in these patients may lead to reactivation, caseation or dissemination of the process

The commonest type of tuberculosilicosis seen in granite workers is that in which there is a very slow progression of the infectious process. Many of these cases appear in patients who have previously shown localized discrete areas by x ray accompanying nodular shadows of simple silicosis,



FIGURE 2

*X ray photograph of the chest of a man working as a hand pneumatic tool operator in granite for fourteen years, showing massive shadows of homogeneous density asymmetrically distributed over areas of mottled nodulation with regions of increased transparency*

*At the original examination this man complained of cough for six years, increasing dyspnea for four years, night sweats for two years and a 15 pound weight loss in two years, examination disclosed bilateral dullness and crepitant rales a sedimentation rate of 18 mm in one hour and, very rarely, a positive sputum*

*He entered the sanatorium three times in four years, each time returning to work after two or three months. He was up and about, though moderately dyspneic, six days before death. There was x ray evidence of cardiac enlargement two months before death*

without silicosis. The primary complex already present is seldom influenced by the inhalation of silica. The lesions are usually healed. They can be reactivated but only rarely. On the other hand, primary infection can occur in patients with silicosis a few weeks after the inhalation of tubercle bacilli. Frequent infection with tu-

and suggesting the occurrence of silicosis superimposed on inactive tuberculosis (Fig 1). The chronic course seems to follow the reactivation of the old lesions, and begins chiefly in the upper lobes and extends to the lower fields. The consolidation increases yearly, and basal infiltration is quite common. There are cough, dyspnea,

distorted thorax and later purulent expectoration. The patients are usually afebrile but have toxic symptoms off and on. The sputum is ordinarily negative until the terminal months, but may be positive intermittently. The x-ray examination may reveal massive consolidation on conglomerate fi

spread complete the story. Some of these patients die with evidence of cardiac dilatation by x-ray, preceded by venous engorgement and ascites.

A less frequent type seen is that which takes a comparatively rapid course with very early cavi-



FIGURE 3

*X-ray photograph of the chest of a man who had worked as a hand pneumatic tool operator in granite for thirty-eight years showing massive homogeneous density in the right upper lung and cavitation and ill-defined nodular shadows in both lungs with greater mottling on the right and increased transparency and loss of fine detail on the left.*

*This man was entirely well up to one month before the first examination when there was sudden onset of cough, expectoration, dyspnea, weakness, nervousness and right chest pain with a 16-pound weight loss in one month. Dullness and crepitant rales were found on the right. The sputum was positive and the sedimentation rate was 24 mm in one hour. At this time he was fifty-seven years old.*

*The symptoms increased with bed rest.*

brotic areas. Later there is peripheral extension and cavity formation which can best be seen in many by overexposure of the film (Fig. 2). The cavities may become invisible to the x-ray and a period of quiescence may follow. Usually progressive fibrosis, cavity formation and a final pneumonic

tion. The onset is sudden with all the toxic symptoms of an acute bronchopneumonia such as productive cough, dyspnea, fever, hemoptysis and rapid weight loss. Serial examinations before and after the onset of acute symptoms suggest that this form of tuberculosilicosis frequently fol-

lows a recent tuberculous infection in a long-standing case of silicosis. The silicosis appears to exert very little influence on the course of the infection, which seems to spread by aspiration as well as by extension. Physical signs are almost always present, and are those of consolidation and cavitation. The x-ray examination discloses mot-

noted in granite workers is that which sometimes occurs among young men. The onset is acute, with marked dyspnea, cough and fever, but there is very little expectoration or loss in weight. Recent x-ray films of the chests of these patients show the nodular shadows of simple silicosis. Films taken immediately after the onset of symp-



FIGURE 4

*X-ray photograph of the chest of the man shown in Figure 3, taken four months later and showing increase in the size and number of the cavities on the right, with irregular distribution of soft mottling in the left lower chest.*

*At this time the patient was markedly dyspneic on the slightest exertion. He died approximately eight months after the onset of the acute symptoms. Autopsy revealed bilateral silicotic nodules, with tuberculous cavitation, in the right upper and lower lobes. In the left lung the alveoli about the silicotic nodules were filled with exudate. Tubercle bacilli were demonstrated in the necrotic areas, almost wholly among the polymorphonuclear leukocytes, none were seen in the silicotic nodules or in the surrounding tissue.*

ting on a nodular background, greatest in the upper lobes, and the presence of rapidly progressive cavitation. The sputum in these cases is markedly positive from the onset of the acute symptoms. The patient rapidly becomes worse with all the symptoms and signs of toxicity, and dies of sepsis (Figs 3 and 4).

A still less frequent form of tuberculosilicosis

toms disclose marked fuzzy borders about the nodules, which increase markedly in size within a few months. There also appears to be rapid coalescence of the nodular shadows. Physical findings at the onset are almost always negative, and one can rarely demonstrate any tubercle bacilli in the sputum. The acute process in these cases may become chronic. This form of tuberculo-

silicosis may be the result of a primary or lymphohematogenous infection in a patient with silicosis and very little resistance to tuberculosis (Fig. 5)

### PROGNOSIS

Patients with silicosis are not certain to develop tuberculosis. Cases of silicosis with early tuber

creasing respiratory symptoms. The continued presence of tubercle bacilli in the worker's sputum carries with it a bad prognosis.<sup>20</sup> Of the 207 granite workers with tuberculosilicosis studied, 20 per cent died within two years after their first examination at which time they were working on full or part time (Table 5). Approximately 87 per cent of those who died and had permitted



FIGURE 5

*X-ray photograph of the chest of a man who had worked as a surface cutter in granite for eighteen years showing a hazy mottling about dense nodular shadows throughout both lungs with well-defined hilar shadows.*

*This thirty-five-year-old man had been examined routinely eight months previously with findings consistent with early silicosis. The tuberculin test (0.1 mg. O.T.) was negative.*

*The present examination was immediately preceded (within approximately five days) by the sudden onset of cough, expectoration, marked dyspnea, hoarseness, and a 2 F temperature rise in the evening. The sedimentation rate was 30 mm. in one hour, the sputum was negative, and the tuberculin test (0.1 mg. O.T.) was positive.*

*On bed rest the dyspnea almost disappeared, but the temperature rise persisted.*

culosis may improve under treatment. The extent and type of the infection regulate the prognosis. In many cases this depends on the amount of previous contact with tuberculosis. The outlook becomes poor with the presence of progressively in

their sputum to be examined showed tubercle bacilli on direct smear (Table 6). Concomitant complications, such as diabetes mellitus, syphilis, and alcoholism, appear to increase the rapidity of the progress of the disease.

PROPHYLAXIS AND TREATMENT

The prophylaxis of tuberculosilicosis consists in the prevention of silicosis and tuberculosis. The prevention of silicosis by the reduction of silica dust in the working environment has proved practical. Pre-employment examinations to detect respiratory disease before the worker can be exposed to silica dust are of value. Regular periodic exam-

TABLE 5 Two-year Progress of Patients with Tuberculosilicosis Working on Full or Part Time at First Examination

TERM OF SERVICE IN GRANITE INDUSTRY	NO OF CASES	DEATHS WITHIN 2 YR AFTER EXAMINATION
yr		%
0-10	5	0
10-20	25	28
20-30	61	21
30 and over	116	18
Total	207	
General average		20

inations lead to the detection of pulmonary infection as early as possible. The removal of all cases with active pulmonary tuberculosis from contact with their fellow-workers can reduce the incidence of tuberculosilicosis.

It must be remembered that a laborer with tuberculosilicosis and a positive sputum can infect not only his fellow-workers but his own children as well. Approximately 70 per cent of all the

TABLE 6 Results of Direct-Smear Examinations of Sputum of Patients with Tuberculosilicosis Dead Within a Two Year Period of Observation

AGE	NO OF KNOWN DEAD	NO PERMITTING SPUTUM EXAMINATION	CASES WITH POSITIVE SPUTUMS
yr			%
20-30	0	0	0
30-40	5	4	100
40-50	10	6	83
50-60	14	11	91
60 and over	12	9	78
Totals	41	30	
Average			87

cases of active reinfection pulmonary tuberculosis found in young people during the period of study in Washington County occurred among the children of men who were ill with or died of tuberculosilicosis (Table 7).

The treatment of tuberculosilicosis is the same as that of pulmonary tuberculosis. The case with the early lesion of infection requires absolute bed rest to determine the stability of the lesion by daily temperature-recording, weekly weighings, sputum examinations and blood studies, and serial physical and x-ray examinations. A period of three to six months is often necessary to determine

the character of the lesion. Collapse therapy often be usefully applied in these early cases.

The more advanced cases are best handled ambulatory methods whenever possible. But common basis of treatment in these cases properly applied and sufficiently prolonged. The duration of the bed rest varies with patient, and cannot be accurately predicted cause of the psychological problems encountered. Many moderately chronic cases show a definite decrease in dyspnea and cough following month of rest in bed. Often, with the return the temperature to normal and the disappearance of toxic symptoms, the patient can get up; start on graduated exercise. Many can be taught the necessary regularity of rest and work. So of these patients after three months in the sanatorium are able to resume work. Following

TABLE 7 Study of Active Reinfection Pulmonary Tuberculosis in Children of Fathers Ill with or Dead of Tuberculosilicosis

Total cases of known active reinfection pulmonary tuberculosis in persons under 40 years of age in Washington County during period of study not engaged in granite work	
Number of these cases with father ill with or dead of tuberculosilicosis	
Sex	
Males	11
Females	34
Age group	
0-9 yr	3
10-19 yr	14
20-29 yr	19
30-39 yr	9

recurrence of their previous debilitating symptoms many return to the sanatorium. Again, after period of one to three months of bed rest, the patient may go back to work. This procedure may last for several years, until continuous bed rest becomes necessary for the marked symptoms which no longer are relieved by any known form of therapy.

SUMMARY

The pathogenesis and the occupational and environmental factors of tuberculosilicosis are discussed. The symptoms and signs and the roentgenological and laboratory findings are described and the clinical focus defined, this being followed by a consideration of prognosis, prophylaxis and treatment.

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## HYPOTENSION THE IDEAL NORMAL BLOOD PRESSURE\*

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**HYPOTENSION** has been looked on as a disease entity ever since the days of Norris<sup>1</sup> who described the "low blood pressure" person as one who lacked stamina, tired easily, complained of cold extremities and showed an inability to do prolonged mental or physical work. "They are not exactly ill yet they are rarely well. This clinical picture of the hypotensive subject has been accepted quite generally,<sup>2-5</sup> and is the syndrome discussed in this paper. We are not concerned with such diseases as Addison's disease, coronary thrombosis, status lymphaticus, shock or infectious diseases which may be accompanied by low blood pressure. The problem we shall attempt to clarify is the state of the individual who has for a long time had a low blood pressure, and who may complain of lack of vitality and fatigue, vague digestive upsets and loss of weight.

### ARBITRARY LEVELS OF HYPOTENSION

The dividing line between normal and hypotensive pressure has never been unanimously agreed on. The upper limit of systolic hypotension has been put as high as 120 mm. and as low as 90 mm. Some authorities notably insurance actuaries, place the limit at a certain percentage below the average for the specific age. These limits are always arbitrary. No writer has ever given a scientific or objective reason for selecting one level in preference to another. Because the 110-mm. level is chosen by about half the observers, we have selected it as the point below which all pressures

are tentatively called hypotensive. We do not imply that this level makes any significant division in the realm of blood pressure. It does not.

The level of diastolic pressure below which hypotension is said to exist is not so frequently suggested. Norris<sup>1</sup> places the limit as high as 80 mm., and Gelman<sup>7</sup> as low as 50 mm. However because the 70-mm. diastolic level corresponds statistically to the 110-mm. systolic level, it has been tentatively selected for the purpose of this report as the upper level of diastolic hypotension.

### INCIDENCE OF HYPOTENSION

Hypotension as just defined is not a rare occurrence. In a sample series of 10,883 persons,<sup>8</sup> representative of an urban group the age-standardized incidence of systolic pressures under 110 mm. was 25 per cent as shown in Table 1 and that of

TABLE 1 Incidence of Hypotension among 10,883 Persons

BLOOD-PRESSURE LEVEL	CAUSE 100% C.	INCIDENCE SUBJECTS TO U. S. POPULATION 1934: AGE 20-74	
		%	N
Under 110 mm. systolic			25.3
478 men	1.9	70.4	
3405 women	38.8	36.0	
Under 70 mm. diastolic			34.1
478 men	30.3	29.9	
3405 women	46.5	43.4	

diastolic hypotension 34 per cent. Although the incidence of hypotension as reported by different authors varies from 2 to 55 per cent there is general agreement<sup>2-5,7</sup> that the incidence is about 20 per cent.

The incidences here given are for all age groups. The well known increased incidence of high pres-

\*From the Department of Medicine, Northwestern University, Chicago, Ill. (Submitted for publication, June 1, 1940).  
 †Presented at the preparation of the paper and edited by the author. (Project No. 455-34 by the personnel of the Work Project Administration, Chicago, Ill.)  
 The author is indebted to the sponsorship of the Institute for Juvenile Research, Chicago, Ill., and to the assistance of Dr. Paul L. Schaeffer, Director.  
 Manuscript in medicine, Northwestern University Medical School, Chicago, Ill., 1940.

tures in the older age groups would necessitate a decrease in the incidence of low pressures In the series just mentioned (Table 2), the age-specific

TABLE 2 Incidence of Hypotension at Specific Ages

BLOOD-PRESSURE LEVEL	AGES IN YEARS											
	20	25	30	35	40	45	50	55	60	65	70	%
Under 110 mm systolic												
7478 men	20	22	24	25	23	22	18	18	14	10	8	
3405 women	56	49	44	42	33	25	25	16	11	11	25*	
Under 70 mm diastolic												
7478 men	43	37	33	29	25	25	22	20	28	29	17	
3405 women	66	59	54	46	38	31	29	26	24	17	25*	

\*Insufficient distribution

incidence of hypotensive persons decreased in the older ages, although the men showed no decrease of systolic hypotension until the age of fifty The incidence of hypotensive women decreased more

per cent) had them Only 2 of the men and of the women had systolic pressures below 80 mm. and 16 men and 23 women had pressures between 80 and 85 mm In the entire group only 31 men and 22 women had diastolic pressures below 50 mm This does not mean that these persons always register such low readings It is more probable that most of them, if studied over a period of years, would be found to be stabilized at the 100-mm or even 110-mm level, and these very low readings probably represent for the most part an exceptional downward dip

The distribution of pressures under 90 mm systolic, 50 mm diastolic over the life span studied brings out an interesting comparison between men and women Considering the age distribution of the total sample, wherein the bulk of the group

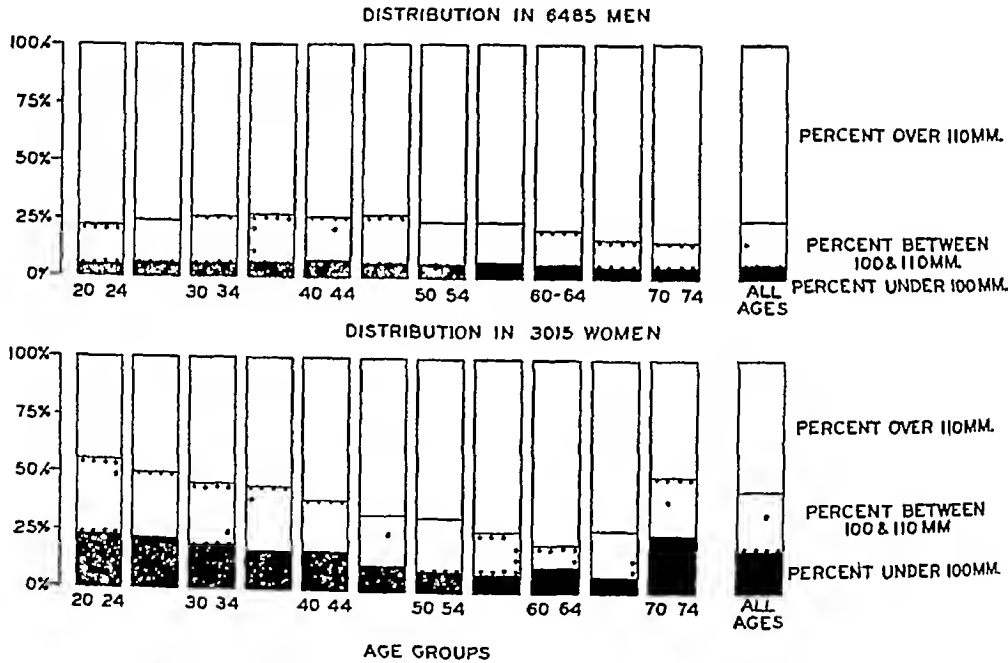


CHART 1 The Incidence of Low Systolic Pressures in a Delimited Group of Adult Men and Women (pressures under 140 systolic, 90 diastolic)

In men there is an almost even age distribution of low systolic pressures Young women show much more low pressure than young men and old women show as much or slightly more low pressure than old men

markedly, but it must be remembered that much of this decrease is due to the unusually high incidence of low pressures among young women If the high pressures are excluded and only those individuals with pressures under 140 mm systolic and 90 mm diastolic are studied, the incidence of hypotension in the remaining more normal group illustrates even better the stability of low pressures throughout the life span (Fig 1)

The occurrence of systolic pressures below 90 mm is rare Of 7478 men, only 42 (0.5 per cent) had such pressures Of 3405 women, only 56 (1.7

was concentrated between thirty and fifty years of age, the men with systolic readings below 90 mm showed no age differentiation (Tables 3 and 4) The frequency distribution of these readings follows that of the total sample. However, among women the low pressures were clustered in the earlier age groups, a distribution similar to that of the entire sample of hypotensive pressures

THE HYPOTENSIVE HABITUS

The person with low blood pressure tends strongly to be underweight<sup>22</sup> Using the ponderal

index\* as a measure of obesity, it is seen that while 30 to 60 per cent of underweight men had systolic pressures under 110 mm., only 10 to 17 per cent of the heavyweight men had them (Fig 2) The underweight men showed from 40 to almost 80 per cent of low diastolic pressure, while the overweight men showed only 11 to 19 per cent.

Women with low blood pressure also tend to be underweight Forty four to 63 per cent of the lightweight women had pressures under 110 mm., while only 15 to 28 per cent of the heavyweight

In the group of slender-build women, 43 to 69 per cent had a systolic hypotension, while only 23 to 33 per cent of broad-build women had it. Also, 53 to 66 per cent of the former women had a diastolic hypotension, while only 29 to 39 per cent of the latter had it

#### EXTENDED STUDY OF LOW PRESSURES

The variation of blood pressure from day to day and from year to year in the same person is an outstanding characteristic of vascular tension To

TABLE 3 *Distribution of Extremely Low Systolic Blood Pressures According to Age*

BLOOD-PRESSURE LEVEL	AGES IN YEARS										TOT. LE
	UNDER 20	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60 AND OVER	
I 478 men:											
Under 80 mm.	0	1	0	0	0	0	0	1	0	0	2
90-94 mm.	2	1	0	6	1	3	3	0	0	0	16
85-90 mm.	1	1	4	1	3	4	2	5	1	2	24
II 3405 women:											
Under 80 mm.	1	0	2	0	0	1	0	0	0	0	4
80-84 mm.	1	1	5	9	3	2	1	0	0	1	23
85-89 mm.	1	6	8	7	3	4	0	0	0	0	29

women had them Similarly 55 to 69 per cent of the lightweight women had diastolic pressures under 70 mm., while only 23 to 35 per cent of the heavyweight women had them

In respect to the build of the hypotensive person as differentiated from his weight, the chest

a large extent the degree of variation, particularly of systolic pressure, is a characteristic of the level of pressure An annual study of blood-pressure readings taken over a span of five to ten years revealed several significant facts It was discovered that the year-to-year variation in blood pressure

TABLE 4 *Distribution of Extremely Low Diastolic Blood Pressures*

BLOOD-PRESSURE LEVEL	AGES IN YEARS										TOTAL
	UNDER 20	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60 AND OVER	
I 7478 men:											
Under 50 mm.	5		4	6	2	2	2	1	0	1	30
50-54 mm.	4	15	21	18	17	10	11	5	4	7	116
II 3405 women:											
Under 50 mm.	2	2	6	6	2	3	0	0	1	0	22
50-54 mm.	14	28	44	39	18	22	8	3	2	2	180

height index is used to delineate the linear or slender build (a low index) from the lateral or broad build (a high index)<sup>23</sup> From Figure 2 it is apparent that the hypotensive person falls in a linear-build classification twice as often as in a lateral build one. Thirty seven to 44 per cent of slender-build men had systolic hypotension, while only 14 to 26 per cent of broad-build men had systolic pressures under 110 mm. Also 35 per cent of slender-build men had diastolic hypotension while only 17 to 21 per cent of broad-build men had it.

was much less among those persons who consistently registered low pressures than among those who consistently registered high pressures Table 5

TABLE 5 *Mean Yearly Variation of Systolic Blood Pressure at Various Levels*

BLOOD PRESSURE LEVEL	No. of MEN	AVERAGE MEAN YEARLY VARIATION
140 mm. and over	28	13.0
130-140 mm.	40	9.9
120-130 mm.	76	9.1
110-120 mm.	116	9.2
100-110 mm.	90	8.0
Under 100 mm.	22	5.7

shows that greater yearly variations were found among the individuals with higher pressures The

ROBINSON, BRUCE AND MANN<sup>23</sup> have shown that weight alone is not a adequate measure of relative underweight or obesity. By dividing weight by height a more practical index of obesity can be obtained. A index number under 2.0 denotes relatively lightweight person, while one higher than 2.4 denotes an obese person.



same is true for diastolic pressures, but to a lesser degree.

Furthermore, the average range of difference between the highest and lowest annual readings was less among those who registered low pressures than among those who had high pressures

pressures over a period of years but seldom experience a rise into hypertensive levels

Thus it is apparent from this study of yearly variation that the dynamic behavior of low pressures is characteristically different from that of high pressures in every respect Both low and high

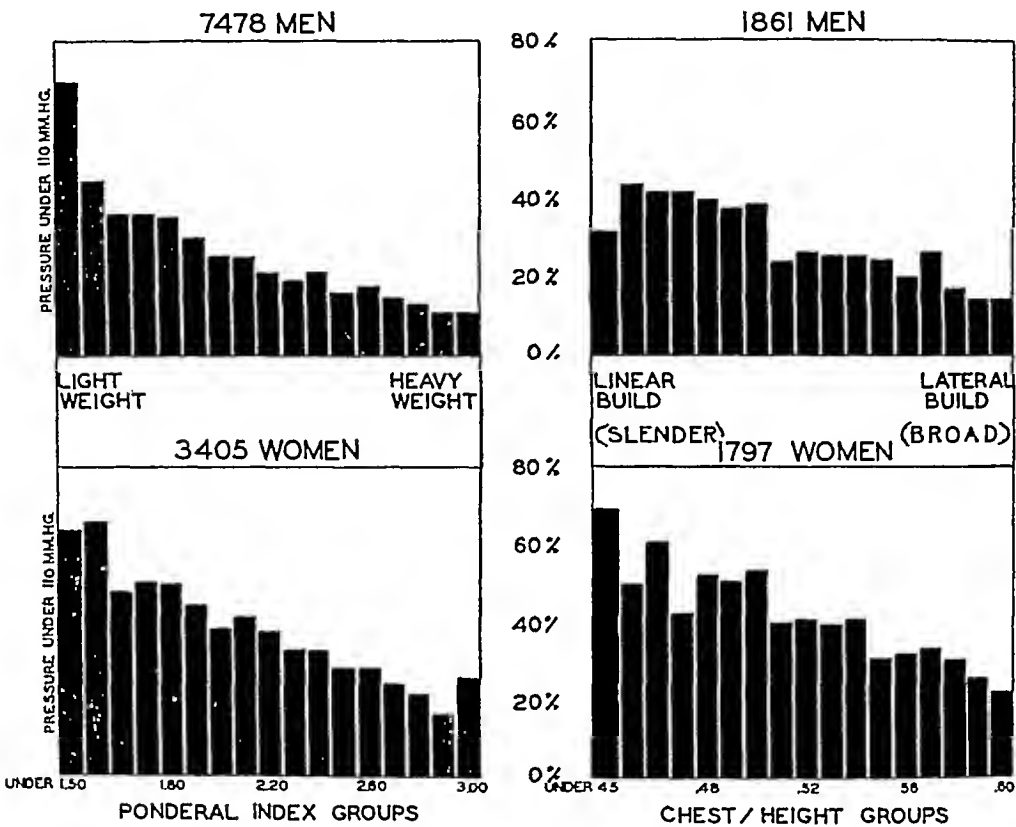


CHART 2 The Incidence of Low Systolic Pressure in Various Weight and Build Groups  
There are many more low blood pressure readings among the lightweight than among the heavyweight men and women There are also more low readings among the linear or slender build than among the lateral or broad build men and women

(Table 6) The diastolic pressure showed a smaller variation between the high and low readings High diastolic pressures showed an average range

TABLE 6 Extremes in Range of Systolic Blood Pressure at Various Levels

BLOOD-PRESSURE LEVEL	NO OF MEN	AVERAGE RANGE OF DIFFERENCE BETWEEN LOWEST AND HIGHEST READINGS OVER A 5 TO-10-YEAR SPAN
140 mm and over	28	26.6
130-140 mm	40	19.0
120-130 mm	78	19.7
110-120 mm	116	19.8
Under 110 mm	112	15.3

of 15.9 mm, while low diastolic pressures showed an average range of only 12.7 mm Finally, it was found that persons with the so-called "hypotensive" pressure, not only tend to keep these

pressures vary from year to year, but high pressures vary to a greater extent than do low pressures, and the variation is more erratic High pressures show a tendency to ascend to higher levels over a ten-year span, while low pressures tend to maintain their level Only rarely does a pressure that dips below 110 mm ascend later to hypertensive levels, or does a pressure that is persistently above 120 mm fail to ascend and become hypertensive (Table 7) Emotion is known to raise blood pressure, but the interesting fact is that persons with low pressures are usually affected very little by these excitations, and frequently not at all

MORTALITY ASSOCIATED WITH LOW BLOOD PRESSURE

The physician should not use the words "normal" or "abnormal" in connection with any physiologic level until he has investigated its associated

mortality. If low blood pressure is abnormal it should be associated with a high mortality. However, most medico-actuarial experience in blood pressure levels speaks in favor of low pressure, as is shown in Table 8. In a recent study by

# THE CLINICAL PICTURE OF THE HYPOTENSIVE PERSON

It is important to remember before condemning low blood pressure that the symptom complex attributed to the hypotensive person was arrived at through a general impression rather than

TABLE 7 Illustrative Records of Low Blood Pressures in Healthy Individuals

Case No.	AGE AT FIRST EXAMINATION	Year													
		1925	1926	1927	1928	1929	1930	1931	1932	1933	1934	1935	1936	1937	1938
1	48	100/70	108/72	106/72	108/70	100/70	108/78	102/70	100/60	100/68	96/70	100/80	103/68	106/74	108/70
2	28			102/62	108/70	106/70	106/68	106/60	120/72	110/70	120/68	110/70	106/72	98/70	
3	32		112/84		114/70	100/60	100/70	102/78	98/70	92/68	100/74	101/74	108/68	92/68	
4	47			100/66	100/66	106/68	100/70	102/72	104/70	90/58	98/66	106/70	100/60		84/58
5	45				100/76		100/68	96/60	110/72	94/60	90/58	90/62	88/60		98/60
6	40			112/72		106/76	102/70	96/69	104/74	106/66	110/60	106/66	106/70		110/60
7	39				106/70	98/72	98/72	96/62	100/66	106/72	108/72	98/64	94/70		94/70
8	47					106/72	102/62	106/60	102/64	94/58	98/66	109/70			98/60
9	39					96/58	102/62	102/64	110/70	102/70	100/66	108/68	94/68	102/60	
10	39				106/70	98/72	98/72	96/62	100/66	106/72	108/72	98/64	94/70		82/54
11	27				110/60	96/66	90/60	100/70	96/64	80/54	96/66	106/70			
12	42					94/64	94/58	90/56	98/68	100/66		102/64		98/60	
13	34				86/60	96/52	100/58	96/50	86/50	82/48					
14	48					98/60	96/62	84/54		104/62		102/58			96/60
15	61				82/54		84/58		80/56	88/52	88/46	88/60		78/42	82/54
16	32				90/54		78/45	94/60		86/58	84/52		80/50		86/58

Hunter,<sup>24</sup> the actual to expected mortality of systolic pressures 13 to 22 mm. below average was 81 per cent, and pressures from 3 to 12 mm. below average showed a mortality of 92 per cent, whereas the average experience was 102 per cent. The

TABLE 8 Mortality of Persons with Low Blood Pressure Levels According to Various Insurance Companies

COMPANY	BLOOD-PRESSURE LEVEL	MORTALITY	
		LOW PRESSURE	VS AGE PRESSURE
		%	%
Northwestern Mutual <sup>25</sup>	100 mm. and under (systolic)	33	80
American Actuarial Society <sup>26</sup>	105 mm. and under (systolic)	47	86
	106 and 110 mm (systolic)	65	86
Metropolitan Life of Canada <sup>27</sup>	10 mm. below average (systolic)	83	100
	15 mm. below average (systolic)	87	100
Joint Committee on Mortality <sup>28</sup>	5 to 15% below average (systolic)	94	100
Prudential Life <sup>29</sup>	Under 70 mm. (diastolic)	49	72
New York Life <sup>30</sup>	16 to 24% below average (mean pressure)	93	97
	5 to 15% below average (mean pressure)	91	97

mortality studies of the insurance companies show that persons with low pressures have a lower mortality rate than have those with average or normal pressures. If the low pressures of the hypotensive group are associated with a more favorable mortality than is any other level of pressure, it would seem, at least from the standpoint of the end result, that the low pressures are the truly ideal ones.

through indisputable clinical statistics. These impressions are easily conditioned by our textbook heritage. For example, consider the common correlation of slender build, low pressure and fatigue. Of all slender-build, lightweight men 44 per cent have a low pressure, and of all broad-chested heavyweight men only 11 per cent have low pressure. Low pressure and slender build are clearly associated.<sup>31</sup> If a physician, trying to associate fatigue with low pressure and build, selected 1000 persons with low pressure for observation, 240 of these persons would be slender while only 60 would be heavy. If in each build group there were the same percentage of fatigue cases, for example 25 per cent, 60 persons would show fatigue associated with low pressure and slender build and only 15 with fatigue associated with low pressure and heavy build. Actually a conclusion from these data would be fallacious, since both the slender and the heavy groups had an equal percentage of fatigued subjects. It would not be fatigue that the physician studied but rather the build-pressure relation. Thus it is seen how the clinical impression of a low pressure, lightweight and fatigue syndrome might develop.

The commonly accepted low pressure symptoms, such as fatigue, headache and dizziness, are widespread complaints; there is no reason to ascribe them to any specific blood-pressure level. In fact they are commoner in hypertensive than in hypotensive patients. A study of fatigue in 100 of five patients showed that 22 per cent of the patients had low pressure, 49 per cent had moderate pressure and 29 per cent were hypertensive. Fahr<sup>3</sup> specifically states that it is usually the

hypertensive patient who notices tiring first. Davis<sup>33</sup> found "headache" to be present in 72 per cent of hypertensive patients. Riseman and Weiss<sup>34</sup> found headache and dizziness a part of the hypertensive picture in over 40 per cent of cases. Marshall<sup>35</sup> found that 62 per cent of hypertensive patients complained of headache, "general weakness" was present in 19 per cent. Ayman,<sup>36</sup> Gager<sup>37</sup> and Christian<sup>38</sup> all list the symptoms of hypertension as others do for hypotension. This is especially emphasized by the statement of

incidental finding in a faulty neuroendocrine and biochemical physiology. Is it possible that the classic picture of the hypotensive person was derived from a study of this rare hypofunctioning type? It is idle, even in this type of patient, to institute any form of therapy directed at raising the blood pressure. Rather, the general condition should be improved by the use of insulin, high vitamins, adequate diet, ultraviolet light, and above all, graduated exercise.

Can the hypotensive person be an active indi-

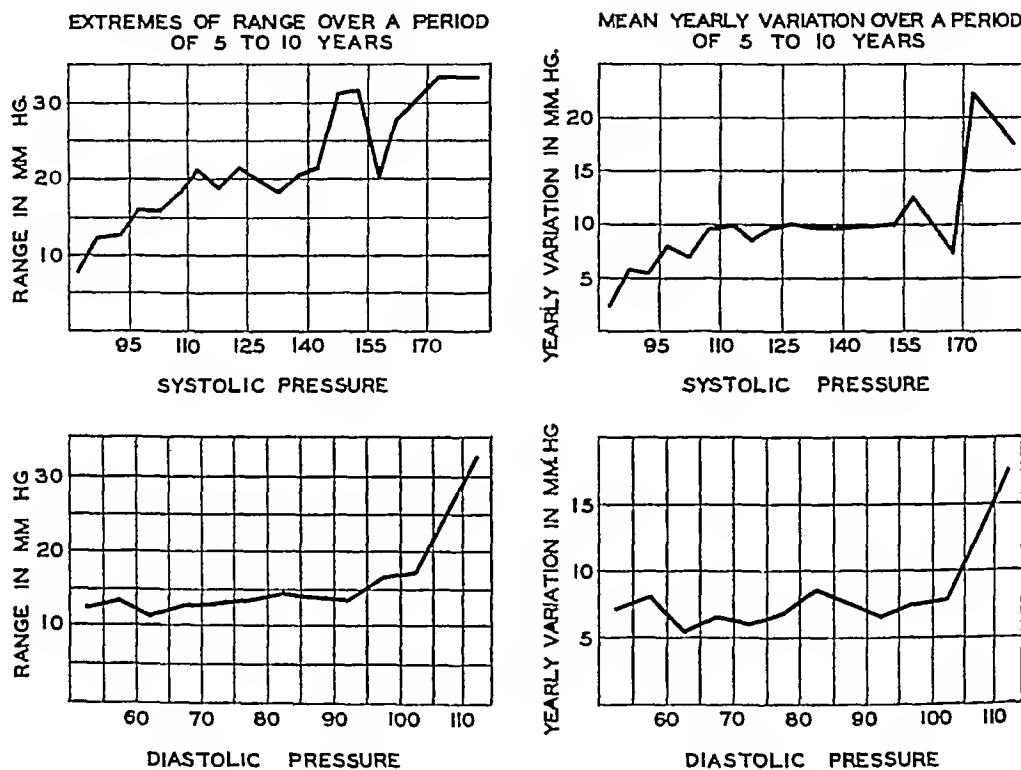


CHART 3 *The Variations of Blood Pressure as the Mean Level Rises*  
*High pressures show less stability than do low pressures*

Kylin<sup>39</sup> "We find, therefore, that the hypertonic and hypotonic symptom complexes are similar in all essentials, except that the blood pressure is abnormally high in the one complex and abnormally low in the other."

We recognize that there are individuals who live in a hypofunctioning state. They may have a low blood pressure. They are nearly always underweight, and have a fragile appearance. They may complain of dyspepsia and nervousness. Their posture is frequently poor, and many are viscerotonic, have a low muscle tone and show evidence of a hypofunctioning glandular system. But these cases are rare and do not represent the typical hypotensive patient. Even in the rare cases of generalized hypofunction the low blood pressure is not the cause of the condition, but is only an

individual, enjoy himself and undergo the rugged issues of life? This question can best be answered by citing some examples.

CASE 1. O. K. M., a 32-year-old man, is 69 inches tall and weighs 150 pounds. He is a teacher of physical education and a coach of athletics; he conducts three daily calisthenic classes, demonstrates with his class on parallel bars, tumbling and horse work, and plays baseball and tennis. His blood pressure on two successive occasions was 98/58 and 98/56. He feels well and has no complaints.

CASE 2. R. J., a 46-year-old man, is 66 inches tall and weighs 155 pounds. He works at the International Harvester Company lifting 85 to 100-pound axles and steel frames into oil for tempering. He does his work fairly continuously all day. His pulse was 84 and his blood pressure 92/60. He feels well and has no complaints.

CASE 3. J. C., a 20-year-old boy, is 69 inches tall and

weighs 195 pounds but does not appear to be overweight. He is extremely muscular and is active in athletics, baseball and track team work. He does physical work but experiences no fatigue, and feels strong and healthy. His blood pressure was 88/58.

CASE 4 A.L.N., a 44-year-old man is 64 inches tall and weighs 145 pounds. He does exceptionally strenuous work carrying loaded milk boxes. His blood pressure on two consecutive occasions was 80/58 and 90/52. He stated that his blood pressure was low 10 years ago.

CASE 5 H.F.J., a 26-year-old man, is 72 inches tall and weighs 172 pounds. His chest circumference is 40

inches and played tennis almost daily. Many similar records can be cited. Further evidence as to the desirability of low blood pressure is found in studies of physically active primitive people.

Nye,<sup>40</sup> studying physically active Australian aboriginals, makes the following observation: "In a general way the constant finding of a low-tension pulse and of arteries of normal appearance was striking. Raised blood pressure and vascular sclerosis were entirely absent in this group of aged primitive aborigines." From this evidence he

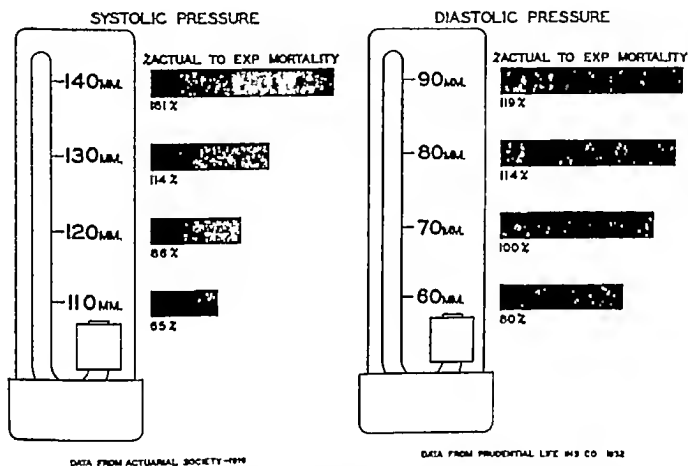


CHART 4 Mortality Trends in Relation to Blood Pressure Readings

This shows for both systolic and diastolic pressures that an increase in pressure is accompanied by a corresponding rise in death rate. The low readings are the most desirable as they are associated with the lowest mortality. (See Robinson and Brucer<sup>41</sup>)

inches and that of his abdomen 32 inches. A ballroom dancer he does exhausting dance steps with lifts, spins and sudden stops, and is especially strenuous in movements in which he throws and lifts his partner who weighs 128 pounds. His blood pressure was 94/58.

Gregory<sup>42</sup> quotes the interesting case of a married woman who consulted him for the first time for her first pregnancy when she was twenty-five years old. She then had a blood pressure of 60 systolic, 45 diastolic. After attending her through three confinements and making numerous blood pressure determinations, Gregory found that at no time except after exercise and during labor, did her pressure rise above 70 systolic, 55 diastolic. The interesting fact is that Gregory describes her as a well-toned active woman who rode every

suggests that hyperpiesia is not a normal condition of senescence. He cites Rowan who found among these same aborigines only 1 case of sudden death and only 1 case of paralysis, in an old man. Donison<sup>43</sup> found low blood pressure at all ages among active East African natives. Hudson and Young<sup>44</sup> found among the Arabs that 72 per cent had blood pressures of 110 mm or under, and noticed relatively few diseases of the circulatory system. Asbford<sup>45</sup> found that the average systolic pressure of Puerto Ricans was well below the standards set in the United States. Fleming<sup>46</sup> made a study of Zuni Indians of New Mexico and found that in general their blood pressures were much lower than those encountered among white people. He was surprised to find many men

of approximately seventy years of age leading lives of extreme physical activity, performing feats requiring great endurance and registering systolic blood pressure between 110 and 125 mm. It should be apparent from this evidence that the classic description of the hypotensive individual has no evidence to support it.

#### RELATION OF LEVEL OF BLOOD PRESSURE TO VITALITY

In the past it has been widely believed that there is a causal relation between low blood pressure and fatigue, and it was consequently assumed that raising of the blood pressure would more adequately nourish the vital organs for more efficient work and greater vitality. As Bock<sup>45</sup> has stated, "Prior to the work of Dale and Richards and of Krogh it was assumed that the pressure of blood in the arterial system constituted the principal mechanism for the provision of an adequate supply of blood to the active tissues." Clinically this pseudo-physiological concept has been carried over to support the contention that the hypertensive is active and energetic because of the high level of his blood pressure, while the hypotensive person is weak, ailing and lacking in stamina because he has not sufficient force behind his blood stream to circulate blood quickly enough for thorough oxidation. Johnson<sup>20</sup> has put it thus: "Hypotension takes so much of the joy out of living that its victim would gladly exchange [it] for the dynamic energy of his neighbor with a higher pressure."

However, it is to be questioned whether either fatigue or the sustained capacity for mental or physical work bears any true relation to the level of blood pressure. This problem has been answered by studies in the physiology of exercise. It has been shown conclusively that sufficient daily physical work raises the efficiency of practically all subjects without essentially altering their blood-pressure levels. This efficiency applies to cerebration and to the subjective state of the individual, as well as to his capacity for physical work. Bainbridge,<sup>46</sup> one of the outstanding authorities in this field, has stated, "Exercise not only leads to a greater sense of well-being, but enlarges the capacity for physical effort and without doubt results in optimum conditions under which the basic processes of life are carried on." Beyer<sup>47</sup> has said, "We sleep better, think better, we react, discriminate and associate ideas quicker, we see, hear and taste more distinctly—as an immediate consequence of exercise."

What are the changes in human physiology that occur when a sedentary subject with a low capacity for work or decreased physical fitness—for example, those with a low Schneider rating—is

transformed by means of daily exercise or work to a better degree of health? These changes may be summarized briefly as follows: the resting pulse becomes slower and there is less increase in pulse rate from the recumbent to the standing position, the pulse and blood pressure increase less with exercise and return to normal more quickly after exercise, the stroke volume of the heart of the active individual is increased over that of the sedentary subject and he requires less oxygen. There is increased lung capacity, increased ability of muscle cells for oxidation and an increase in the capillary bed.<sup>48-54</sup> All these changes are accomplished, according to most observers,<sup>45, 46, 55</sup> without raising the resting blood pressure. In fact, some observers<sup>56-59</sup> have found that the blood pressure and pulse are lowered as physical fitness increases.

From the foregoing it is clear that low blood pressure does not cause fatigue and lessened vitality, any more than high blood pressure causes an increase in physical efficiency. The degree of health or mental and physical fitness is not an attribute of blood-pressure levels, rather it is dependent upon cellular oxidation and biochemical changes and these, in turn, aside from hereditary differences, are to a great degree dependent upon the extent of daily work an individual performs.

The physiological differences between the active and the sedentary person are of the greatest biological importance to man. They represent intrinsic and deep-seated advantages to the active person, all of which ultimately lead to a greater capillary bed and a greater utilization of oxygen by the tissues, measurable long after activity has stopped. These protoplasmic differences between the confined and active human being play a role in most of the degenerative diseases. Modern civilization, which imposes sedentary living on most city-dwellers, is the real cause for fatigue and lack of vitality, regardless of the level of blood pressure. Low blood pressure is found to be common in physically active persons such as farmers, primitive peoples and athletes, yet persons in these groups do not commonly complain of fatigue. It is easy to single out hypotension as the etiologic cause in any given patient's many complaints, because it is so easily and quickly measured. However, in most cases of fatigue and lowered vitality, regardless of the level of blood pressure, if we were to inquire further we should find a sedentary worker confined to a poorly ventilated office or shop, smoking a package of tobacco daily, riding to and from work, taking his recreation as a passive spectator rather than as an active participant and with practically no out-

door exercise. Fatigue and a condition below par more truly belong to such a combination of living habits, and are not to be attached specifically to one convenient cause, hypotension.

This may be well illustrated by the following thirty-five year history of a Chicago attorney with so-called "hypotension." He is now fifty four years of age, 69 inches tall, and weighs 149 pounds. His chest measurement is 34 inches, that of the abdomen 31 inches. He first learned of his low blood pressure in 1905 when as a student in college he was examined for participation in athletics. He was told that his systolic blood pressure was 104 mm. The examining physician, who was doing some research in blood pressure, checked him carefully for three months. His pressure was persistently low during this period, although he was allowed to participate in track and scrub football. He has been examined annually ever since, and his blood pressure has been constantly low. An examination each year since 1913 has shown that his systolic pressure has never exceeded 112 mm. Although he had never been sick in his life, he complained of fatigue and a "loggy feeling" and lacked energy. He would fall asleep in the evening after dinner while reading the newspaper, and yet suffered from insomnia. In 1926 he bought a home with a large lot in the suburbs. He did all his own work, spaded cut the grass, shoveled snow, bought a complete set of carpenter tools and did all the work around the house. He and his neighbor put up a steel wire fence and sank the posts in concrete. He insulated his own garage and that of his neighbor. He does some physical work every week day and all day Saturday and Sunday. Since he has become physically active he does not have any more fatigue. He can work through a twelve hour day and still be on his toes all the time; his mind is clearer. With this subjective improvement of his health and greatly improved capacity for mental and physical work, his blood pressure remained unchanged. It was 98 mm systolic, 68 mm diastolic on September 20, 1939 and his pulse was 68.

This person was cured of his fatigue, low vitality and insomnia not by raising his blood pressure but by daily physical work. Just as low blood pressure cannot be blamed for the fatigue of the underweight person, high blood pressure (except extreme readings) cannot be held responsible for the fatigue of the obese person. Fatigue is not a function of the level of blood pressure; it is rather a deep-seated metabolic dysfunction most often related to inactivity.

#### BLOOD PRESSURE BELOW 90 MM. SYSTOLIC

Robinson and Brucer<sup>40</sup> have shown in a previous paper that blood pressures between 90 and 120 mm. were in the range of the normal. What about pressures below 90 mm.? Are they normal?

In the first place, we wish to distinguish two types of pressures at this level. There is the individual with a history of systolic pressure stabilized around 100 or even 110 mm. whose pressure in the course of a ten year span occasionally dips below 90 mm. In many cases these occasional deviations can be accounted for. For example, the individual in Case 4 (Table 7) had a blood pressure stabilized over a twelve year span at about 100 mm. systolic. In 1938 his level dropped to 84 mm., but this was a temporary fall following illness. We know that blood pressure falls during and following infectious diseases, especially in influenza, and may stay low for a period of a few weeks or more. Hence, an occasional reading considerably below one's stabilized blood-pressure level may be caused by any acute illness, and is not a reflection of the intrinsic pressure of the individual. Such cases constitute the majority of systolic readings below 90 mm. The history of pressure just cited is definitely normal, as is shown from continuous studies of records and of mortality data.

Second, there is the individual whose history over a ten year span shows a systolic blood pressure usually below 90 mm. Is this blood pressure normal? There is nothing in the literature to prove that it is abnormal, and all the phases of our study would indicate that it is normal. In the first place, there are very few such persons available for study. We have encountered only 4 out of the 500 persons in our continuous study covering five or more years. These individuals were enjoying good health and were actively at work. The literature contains other such records. If it is a fact that these persons are in good health and do not complain, and if their life expectancy fits in with what has been demonstrated for low blood pressures generally, there is no reason to look on these very low blood pressures as pathologic. Until evidence to the contrary is presented, we are practically compelled to accept this viewpoint.

#### SUMMARY AND CONCLUSIONS

Between one fourth and one third of the adult population have blood pressures under 110 mm. systolic and 70 mm. diastolic. Such blood pressures are usually designated as "hypotension."

Age has a negligible effect on the distribution

of low systolic blood pressure in men up to the seventh decade, thereafter the incidence decreases. Young women have a much higher incidence of low blood pressure than do men, and old women have about the same incidence as do old men.

Hypotension is commonest among the linear-built or narrow-chested type of build.

It is two or three times commoner among lightweight than among heavyweight men and women.

Low blood pressures show a smaller and less erratic yearly variation, and do not vary over as great a range as do high pressures.

They do not tend to rise with age, rather they maintain an even level.

They are associated with a mortality rate lower than that of average pressures.

The symptoms usually ascribed to hypotension are in reality commoner among hypertensive persons. There are no symptoms peculiar to or due to low blood pressure.

Neither fatigue nor vitality is a function of the level of blood pressure, rather they are related to the daily physical activity of the individual. In fact, those persons noted for endurance, vitality and well-being, trained athletes, farmers and other active groups, are also noted for their high incidence of low blood pressure.

Hypotension is not a disease, it is an ideal blood-pressure level.

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## CLINICAL NOTE

## A SYMPTOM OF ONE-SIDED AFFECTION OF THE LUNGS AND OF THE MEDIASTINUM

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IN MANY cases of chronic affections of the lung, pleura and mediastinum (basal pleuritic adhesions, chronic pneumonias, affections of the hilum lymph nodes, tumors of the bronchi and *Pleura kappe*), I have very often witnessed a symptom which Pottenger<sup>1</sup> observed many years ago. Whereas in cerebral hemiplegias the protruded tongue deviates toward the opposite or paralyzed side,—for example, in the lesion of the left cerebral hemisphere the right half of the body is paralyzed, with deviation of the tip of the tongue to the right,—in affections of one side of the lung or of the mediastinum the tip of the tongue deviates to the affected side. The half of the tongue corresponding to the affected side is smaller than the other half. Sometimes there is a slight fibrillary twitching of the muscle fibers, and the border of the tongue may be shallower on the deviated side. No sensory defect can be detected in either the anterior or the posterior part of the tongue.

Since hemorrhage into the internal capsule involves supranuclear hypoglossus fibers situated close to the genu (geniculate fibers), there results a paralysis of the hypoglossus on the same side as the paralysis of the body muscles. This paralysis is characterized by deviation of the tip of the tongue to the paralyzed side since the normal musculature of the opposite genioglossus muscle pulls the tip of the tongue forward and at the same time toward the paralyzed side.

Cortical lesions present the same symptoms so far as the paralysis of the musculature of the body of the tongue is concerned. In severe cases of cellulitis of the neck there may result a periph-

eral paralysis of the hypoglossus nerve, due to phlebitis or periphlebitis of the jugular and facial veins. In toxic neuritis—that caused by the ingestion of lead, arsenic or alcohol—a peripheral toxic paralysis of the hypoglossus nerve may result which escapes the observation of the patient because the intervening of the muscle fibers of both halves of the tongue prevents any functional disturbance.

For the interpretation of the above mentioned sign, two factors may be considered. First, the underlying inflammatory or neoplastic condition of the lung or surrounding tissues may produce a hematogenous damage to the hypoglossus nerve on one side. (Chronic polyneuritis combined with muscular atrophy is not uncommon in chronic pulmonary tuberculosis.) The fibrillation of the muscle fibers of the tongue could be interpreted in this manner, since in toxic neuritis myokymia is not uncommon. As swelling of the lymph nodes in the mediastinum, in the neck and at the base of the skull in chronic pulmonary affections is not rare, a compression of the hypoglossus nerve by a lymph node could be possible.

Since the atrophy of one half of the tongue and the deviation of its tip correspond regularly to the position of the affected lung, a reflex may be significant. Afferent vagus fibers from the lung irritated by the chronic process within the thorax might transmit the irritation to the hypoglossus nerve, since anastomoses between the vagus and the hypoglossus nerves, after the latter has left the hypoglossal canal, and between the hypoglossus nerve and the ganglion nodosum are common.

The syndrome of deviation and atrophy of one side of the tongue seems to belong to the old vegetative, accompanying symptoms of chronic lung diseases, such as Horner's syndrome, atrophy of the trapezius muscle of one side, redness of the cheek, difference between pupils and so forth. The syndrome is of diagnostic value.

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## REPORT ON MEDICAL PROGRESS

## PEDIATRICS\*

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## TETANUS TOXOID

ACTIVE immunization against tetanus among selected groups has been employed for several years in certain European countries. Those receiving this treatment have been persons whose duties necessitated frequent exposure to infection. The results of this type of prophylaxis have been so satisfactory that several observers in this country have been stimulated to make further observations.

Active immunization may be obtained by the subcutaneous or intramuscular injection of tetanus toxoid, plain or alum-precipitated. The latter is more slowly absorbed and hence exerts an antigenic stimulus over a longer period of time. For this reason it has been considered by most observers to give a higher antitoxic response than does plain toxoid.

The studies of Gold,<sup>1</sup> Bergey and Etris,<sup>2</sup> Hayden and Hall<sup>3</sup> and others have shown that the highest antitoxic response is obtained when the injections are given at intervals of two or three months rather than two or three weeks. In fact, Jones and Moss<sup>4</sup> have shown that even a smaller total quantity of tetanus toxoid given at wide intervals produces a higher and more prolonged antibody response than does a larger volume given at a single injection. These observations are similar to those noted by Benjamin, Fleming and Ross<sup>5</sup> in a study of 5195 children who had received injections of diphtheria toxoid. It would therefore appear that the proper procedure is to give an initial intramuscular injection of 1 cc of alum-precipitated toxoid and to repeat this dose either two or three months later.

There is very slight antibody response to the initial injection of toxoid, and it is only after the second injection that a satisfactory response may develop. In a study of 34 adults, Gold<sup>6</sup> showed that the tetanus antitoxin content of the blood fell rapidly during the first three months following the second inoculation, reaching less than 0.01 units per cubic centimeter of blood serum. In a subsequent study the same author<sup>7</sup> concluded that the minimal antitoxic value for

protection should not be below 0.1 unit per cubic centimeter of blood serum. These observations are in accord with those of Hayden and Hall, who immunized 152 volunteers from the United States Military Academy. Six weeks after the first injection the tetanus antitoxin content of the blood rose from an untitratable quantity to one of about 0.01 unit per cubic centimeter, and eight weeks after the second injection to 0.40 unit. All observers agree that the content falls rapidly during the first few months following the last injection. However, an extraordinarily rapid increase in tetanus antitoxin content occurs following a third or stimulating dose, the level reaching as high as 10 or more units per cubic centimeter. This is more than would have been present following the administration of a prophylactic dose of antitoxin, and its presence is therefore of therapeutic value.

This antitoxic response develops in six to eight days following the injection of the third or so-called "stimulating" dose, and hence falls within the usual incubation period of tetanus. Such results, however, should not be expected when the inoculation is given sooner than one month after the second prophylactic injection. Also, as pointed out by Gold, this procedure is of no value if employed between the first and second immunizing vaccinations.

Recently a biological product has been made available which contains both diphtheria toxoid and tetanus toxoid. Hence the possibility of immunizing individuals, especially children, to both diseases presents itself. The question of the advisability of the administration of more than one antigen at the same time arises, in an effort to answer it, a large amount of experimental data has been accumulated. These data indicate that the antibody response to each antigen when two or more are employed is as high, and as prolonged, as when only one is injected. Jones and Moss<sup>8</sup> studied the antitoxic titers of 41 students at the Indiana University School of Medicine who received combined diphtheria and tetanus toxoid, and obtained results indicating not only that the combined use of the two toxoids was feasible, but that immunity to both diseases could thus be established. In a study of the same group one year later, it was shown that immunity to diph-

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theria had been satisfactorily established and that the response to the third or stimulating injection of alum-precipitated tetanus toxoid increased "the antitoxic content of the blood twenty to fifty times, making a level which is higher and more persistent than that produced by a prophylactic injection of tetanus antitoxin." From these studies it would appear that the combined use of the two toxoids produces a satisfactory immunologic response and is therefore of prophylactic value.

The universal administration of alum precipitated tetanus toxoid, either alone or in combination with alum precipitated diphtheria toxoid may not be acceptable to all physicians concerned with the care of infants and children. In fact there may even be certain objections to such a procedure. However, the administration of tetanus toxoid to all infants and children who are known to be allergic or who have previously received a dose of horse serum and are therefore probably allergic to it, or who are repeatedly being exposed to possible infection, appears to be advisable. Neither anaphylaxis nor serum sickness is agreeable. One should realize that there is a definite individual variation in the degree of antitoxic response to the injection of tetanus toxoid and that as yet there is no clinical test like the Schick test for diphtheria, by means of which this response may be determined, titration of the blood serum is the only means. Therefore, if a patient who has previously received two injections of toxoid is wounded under circumstances indicating that tetanus spores are likely to be present in the wound it is better to give not only 1 cc of tetanus toxoid but also a prophylactic dose of tetanus antitoxin.

#### ACUTE ANTERIOR POLIOMYELITIS

It is an irrefutable fact that the diseases which are accompanied by disabling sequelae attract the greatest interest. To date one may truthfully say that infantile paralysis continues to occupy a prominent position among such conditions. Furthermore, it is unfortunately true that our knowledge concerning any specific form of therapy to be applied during the acute stage of this disease is embarrassingly scanty. However an understanding of the epidemiology of the disorder, and particularly of the mode of dissemination with possible subsequent infection may easily be a more effective measure in the control of acute anterior poliomyelitis than are drugs. Certainly this seems at present to be the most promising approach.

For many years it has been the common belief that the virus of acute anterior poliomyelitis enters and leaves the body through the respiratory passages. Recently attention has once more been focused on the possible presence of the infecting

agent in the stools of patients with the disease, of convalescent patients and of persons without the disease who have been in contact with patients so infected. Harmon<sup>9</sup> in 1937 and Trask and his co-workers<sup>10</sup> in 1938 successfully demonstrated the presence of the virus, thus reaffirming earlier observations. In a later report the latter authors<sup>11</sup> studied thirteen stool specimens obtained from 8 patients and were able to isolate the infective agent in three specimens all obtained from the same patient. It is significant that this patient did not have paralytic poliomyelitis (as his brother had at the time) but was suffering from the abortive form of the disease. As the authors point out such a diagnosis might not have been made had not the virus been found. It was present in the stools as late as the twenty fourth day after onset of the illness, thus demonstrating how long the patient might have served as a source of infection to others. A specimen of the stool preserved in a refrigerator for ten weeks showed the virus to be still viable. Successful recovery of the virus from feces has been reported also by Kramer<sup>12</sup> Toomey<sup>13</sup> and Lepine.<sup>14</sup>

Kramer Gilliam and Molner<sup>15</sup> while studying an outbreak of the disease in a children's home in Detroit during the summer of 1939 were able to demonstrate the presence of the virus in the stools of 6 out of 19 persons who were not suffering from the infection but had been in contact with 5 patients who were. In one of these healthy persons the virus persisted in the stools for nineteen days following its first detection and in another for thirty-eight days. Although it cannot be proved that these 6 people acquired the virus from the ill patients, it is reasonable to assume so. Thus it would appear that during an epidemic the patient is not the only source from which infection can be disseminated.

These recent observations may be of real epidemiologic significance and naturally open further fields for study. From the practical aspect consideration should be directed toward the proper disposal of the intestinal contents of all patients suffering from acute anterior poliomyelitis, a precaution which probably has not been considered very seriously in the past. Similar disposal of the feces of all healthy persons in contact with an ill patient would hardly seem practicable and certainly is not so where large groups or institutions are concerned.

Since the virus may be present in the gastrointestinal tract of those who present no evidence of infection as well as of those ill with the disease the question of sewage is a possible mode of dissemination arises. Paul Trask and Culotta<sup>16</sup> studied specimens of sewage obtained from dif-

ferent locations in the city of Charleston, South Carolina, during the summer epidemic in 1939 and were able to isolate the virus. In fact, their results demonstrated massive contamination of the sewage. Such observations naturally attract the attention of public-health officials as indicating a potential danger, indeed, the condition may exist in small localities or in situations where adequate sewage disposal is difficult. However, in most instances the sewage would be diluted to such an extent that the possibility of infection from this source would be reduced to a minimum. Naturally one would not advocate bathing in a small stream or body of water into which the city's sewage emptied. In view of our present knowledge, such procedures should be prevented during an epidemic. When one considers the large number of people attending the public beaches during the summer months, one cannot help but wonder if the chance of infection from spray-borne material from unrecognized carriers is not greater than that of infection from pollution of the water.

#### PNEUMOCOCCAL PNEUMONIA

In the 1939 progress report,<sup>17</sup> attention was directed to the use of a new agent, sulfapyridine, in the treatment of pneumococcal pneumonia. Since that time another medium of chemotherapy has been offered which appears to possess many features that render it preferable to sulfapyridine. This new drug, sulfathiazole, is now commercially available. Its addition to our armamentarium gives us three forms of specific therapy for the treatment of pneumococcal pneumonia, antipneumococcus serum, sulfapyridine and sulfathiazole.

When so many promising procedures are available for the treatment of a disease, some confusion may result as to which is the best one in a given case. Blake<sup>18</sup> has recently analyzed the results obtained from the three drugs mentioned, and has pointed out the varying factors observed in the clinical response to each. He studied 250 cases of pneumococcal pneumonia treated at the New Haven Hospital. One hundred and nine patients received sulfapyridine alone, 41 sulfapyridine and antipneumococcus serum, 97 sulfathiazole alone and 3 sulfathiazole and antipneumococcus serum.

The 150 patients receiving sulfapyridine alone included 45 on the Pediatric Service, the rest were over the age of thirteen, the age limit for this service. Age appeared to be one of the most important factors in determining the outcome. Ninety-five per cent of the children were under ten, and only 3 per cent of these showed relapses, complications or fatal terminations following therapy. Unfavorable reactions, such as persistent

low-grade fever, complications and death, paralleled the increase in age.

The results from treatment with sulfapyridine and antipneumococcus serum (41 cases) showed little if any difference from those obtained from sulfapyridine alone, and whatever difference was noted was in favor of the latter. However, a study of the results in this group discloses two striking facts, namely, that there were few patients under ten years of age, and that many cases suffered from an accompanying bacteremia. These are indeed important factors for a final appraisal of the statistics.

In the group of 100 patients who received sulfathiazole, the results were similar to those obtained with sulfapyridine alone, the difference again being dependent on age. As in the other groups, older patients who were suffering from Type 3 pneumococcal pneumonia showed a tendency to recover less rapidly than did those suffering from other types. A final study of the factors influencing mortality revealed that old age, with its accompanying incidence of chronic disease was more important than bacteremia, the type of pneumococcus or the time, that is, day, relation of the institution of specific therapy to the duration of the illness.

The value of anti-pneumococcus serum in the treatment of pneumococcal pneumonia is beyond question. However, in dealing with specific forms of treatment in this disease, one must bear in mind that the prognosis of acute primary or lobar pneumonia in infancy and childhood differs from that among adults. Prior to the introduction of specific serum the mortality rate of this type of pneumonia among infants under two years of age was discouragingly high. Curnen<sup>19</sup> reports that in a series of 50 infants suffering from Type 14 pneumococcal pneumonia who received serum there were no deaths—a fact which he took to prove the value of this form of therapy. Yet no one who has administered serum to infants is unaware of the reactions, not including serum sickness, which often appear. Davies<sup>20</sup> observed equally good results when sulfathiazole alone was used in the treatment of 150 infants and children suffering from pneumococcal pneumonia. In this group, practically all recognized types of pneumococcus were encountered. This is a significant feature, for not infrequently many types of pneumococcus are present at the same time, a finding which makes it difficult to decide which type of serum to administer. Among infants with pneumonia, Type 14 is most commonly encountered, whereas in children over two years of age, Type 1 is usually the predominating organism. However, with rising age there is an increase in the number of types of organism present, and this of course

renders specific therapy with serum somewhat confusing. Fortunately, the use of sulfapyridine and sulfathiazole has obviated this difficulty. Davies' study showed that the temperature returned to normal fairly promptly, and that the majority of the patients were restored from a critically ill state to one of comparative comfort within twenty-four to forty-eight hours after treatment was instituted. This should not be misconstrued as necessarily implying that the clinical or roentgenologic evidence of pulmonary involvement disappeared in as short a period of time.

The dosage as well as the manner of administration of sulfathiazole is similar to that employed with sulfapyridine, that is,  $1\frac{1}{2}$  gr per pound of body weight as the initial dose, followed by 1 gr per pound per day, usually divided into six doses and administered every four hours, as the daily maintenance dose. In cases in which nausea is present it is advisable to divide the initial medication into two parts, giving half the total amount each hour for two doses. This produces a blood level between 4 and 11 mg per 100 cc., which in most cases proves therapeutically effective.

Untoward, toxic manifestations, such as nausea, vomiting, fever, eruptions, hematuria and neutropenia, have been much less frequently encountered with sulfathiazole than with sulfapyridine. This fact, together with the clinical evidence that sulfathiazole is equally as effective as sulfapyridine, has made treatment with the former the procedure of choice for pneumococcal pneumonia occurring among infants and children.

### INFLUENZAL MENINGITIS

Although the administration of anti-influenza horse serum has to some extent reduced the mortality rate of influenzal meningitis, the results are far from satisfactory. The introduction of chemotherapy naturally prompted some investigators to try this type of treatment, although an occasional recovery has been reported,<sup>1</sup> failures are not unknown.<sup>2,3</sup> At the present time there is insufficient data even to suggest that this form of therapy will prove effective. The most promising type of treatment has recently been offered by Alexander and Heidelberger,<sup>4,5</sup> who have prepared a successful anti-influenzal serum from rabbits. This possesses a smaller anti-carbohydrate molecule than does anti-influenza serum prepared from horses, and hence has greater power of penetrating the tissues. The specificity of this serum for Type B strains of *Hemophilus influenzae* can be demonstrated by microscopic studies executed in a manner similar to the typing of pneumococci by the Neufeld method. Dr. Alexander kindly furnished this serum for the treatment of 3 patients suffering from influenzal meningitis at the Infants

and Children's Hospitals,\* and 2 of these patients recovered. The third child was moribund at the time of admission and died within a few hours.

It is well recognized that the mortality rate of this disease is influenced not only by age but also by season, so that care must be exercised in drawing conclusions too hastily. That such care is being exercised is clearly shown in the following statement by Alexander:<sup>6</sup> "While the number of patients treated is still very limited the serum has been used with promising results in several clinics. When all types of cases are included even those dying within less than twenty-four to forty-eight hours of admission, the resultant mortality has been approximately 50 per cent." Certainly such results justify further use of this type of anti-influenza serum.

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\*This serum is now available commercially through E. R. Squibb & Sons, New York City.

## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

### CASE 26371

#### PRESENTATION OF CASE

An eighteen-year-old Jewess was admitted to the hospital complaining of intermittent joint pain.

The patient was well until nine months before admission when she awoke one morning to find "a funny aching pain" in both knee joints, made worse by exercise. So far as she could recall, the knees were not swollen, red or hot, and the pain was transient, having periods of exacerbation and remission. She went to bed for a week, rested two more, and then returned to school, entirely free of joint symptoms. She engaged in normal scholastic athletics, such as bowling and gymnasium exercises, without joint discomfort. She was free of symptoms for about two months, then, approximately seven months before admission, she again began to have pain in the knees, with occasional puffiness and tenderness to touch and movement, but with no noticeable redness of the overlying skin. She soon experienced similar discomfort in the wrists and proximal phalangeal articulations. The wrists caused so much pain for a short while that she taped them with adhesive in the belief that they were sprained. Small red spots appeared at the sides of several of the involved proximal joints of the fingers. Following this the ankles, elbows and wrists intermittently became tender and painful on motion. The attacks of pain were transient, lasted only a few days and tended to involve one joint after another. Although never considered a sickly girl, she had been extremely susceptible to upper-respiratory infections. She had had a tonsillectomy in infancy. There was no history of nosebleeds, rheumatic fever or chorea. Familial diseases included "arthritis" in a maternal uncle and grandfather, and hay fever in a maternal aunt. The remainder of the past and family histories was non-contributory.

Physical examination revealed a well-developed and well-nourished girl who lay quietly in bed in no discomfort. She had a rather dusky color, there was no pallor of the mucous membranes. The heart was not enlarged, the rhythm was regular, the rate being 142. The sounds were of fair quality. There was a faint, apical systolic murmur and a roughening of the pulmonic second

sound, which was louder than the aortic second sound. The blood pressure was 126 systolic, 72 diastolic. Examination of the lungs was negative. The liver was palpated a handbreadth below the costal margin, and the tip of the spleen was felt. Pelvic examination was negative. There was a slight right upper and left lower dorsal scoliosis. Difficulty was experienced in fully extending the fingers of the right hand, but no limitation of motion of any other joints was noted but there was pain on moving the knees and elbows. Both feet and lower legs were colder than the remainder of the body. Epitrochlear lymph nodes were palpated, but no rheumatic nodules were noted.

The temperature was 101°F., the pulse 120, and the respirations 24.

Examination of the blood showed a red-cell count of 4,200,000 with 74 per cent hemoglobin, and a white-cell count of 8800 with 64 per cent polymorphonuclears, 15 per cent lymphocytes, 4 per cent monocytes and 17 per cent eosinophils. The platelets were normal. The urine examination showed a specific gravity of 1.038, with 10 to 20 white blood cells per high-power field in the sediment, there was no albuminuria. The stools were guaiac negative. A blood Hinton test and a gonococcal complement-fixation test were negative. Frequent blood cultures were negative. The blood sugar was 92 mg per 100 cc., the serum protein 6.9 gm, the serum albumin 3.2 gm., and the serum globulin 3.6 gm or an albumin-globulin ratio of 0.89. The serum nonprotein nitrogen was 17.2 mg per 100 cc., the serum calcium 10.2 mg., the serum phosphorus 3.9 mg., and the uric acid 3.7 mg. A sedimentation rate in fifteen minutes was 20 mm, thirty minutes, 49 mm, forty-five minutes, 54 mm, sixty minutes, 56 mm. An electrocardiogram showed a ventricular rate of 95 with normal rhythm, a slight tendency to left-axis deviation, a complete inversion of Lead 3, but an otherwise normal record.

Roentgenograms of the hands and knees showed slight soft-tissue thickening about the interphalangeal joints of both hands. The cartilage spaces, however, were of normal width. The articular surfaces were smooth, and the bones were not remarkable. The bones of both knee joints showed no definite variations from the normal. A chest plate showed that the heart shadow was at the upper limits of normal. The heart was broad across the base, and there was definite prominence in the region of the left ventricle. The lung fields were clear. The diaphragm was normal in position and outline.

The patient ran an almost constant, slightly elevated temperature (around 100°F.), with a

slightly elevated pulse (about 110) and respirations which varied from 22 to 25. After a few weeks in bed she began to ooze blood from the nose and mouth. It was then found that the blood clotting time was 40 minutes, and the bleeding time  $13\frac{1}{2}$  minutes, a tourniquet test was positive, with many petechiae. The platelets were normal in number, and the clot retraction was good at 4 and 12°C. The prothrombin value was 32 per cent of normal, and the anathrombin factors were greatly increased. The hematocrit was 34 per cent. The plasma vitamin C determination was 0.29 mg. per 100 cc., and the total carotinoids were 0.04 units per cubic centimeter (the normal being 2 to 4 units). Vitamin A determinations showed 0.6 units per cubic centimeter (the normal being 1 to 4 units). These findings indicated a deficiency in vitamins A, C and K. She was given large quantities of vitamin concentrates, with methyl naphtholquinone and dioxy cholic acid by mouth. Later, methyl naphthol quinone was given parenterally and she was transfused. With this treatment she ceased oozing blood, but three to four weeks later the symptoms recurred and required further vigorous though similar therapy.

The liver and spleen became progressively enlarged. A cervical lymph node removed for biopsy showed hyperplasia. An aspirated specimen of the sternal bone marrow was normal. A biopsied piece of muscle showed no diagnostic abnormality. Blood smears continued to exhibit a relatively high eosinophilia 22 per cent on one occasion. A van den Bergh test showed 41 mg. bilirubin per 100 cc. There was a Congo red retention of 67 per cent, a bromsulfalein retention of 40 per cent, a +++ Takata-Ara test, bilirubin, hematuria, a basal metabolic rate of +18 per cent, normal blood sugar, a normal hippuric acid excretion and a negative 17 ketosteroid determination. An undulant fever agglutination test and tests for kala azar were negative.

A transient but definite pericardial effusion developed and slowly receded during the middle of her hospital stay. She developed a chronic mouth infection and seemed to be in extremis on two or three occasions, with high temperature, great prostration and mental disorientation. On each occasion she rallied and seemed to return almost to her former fair health. At one time she developed a rash on the hands, the left elbow and the buttocks. This rash consisted of irregular erythematous patches which were not infiltrated over the buttocks but which showed definite thickening and infiltration elsewhere. She slowly but gradually failed, became dyspneic and had irregular respirations. About two weeks be-

fore death she developed diarrhea. At that time proctoscopic examination showed a "dry" glazed mucosa with a tenacious adherent brownish discharge becoming more liquid as one proceeded upward to the level of the rectosigmoid junction. The swabs removed at proctoscopy were guaiac positive. No discrete ulcerations or polyps were observed. The abdomen became distended and tympanitic, with rare peristaltic sounds. The liver and spleen continued to become more palpable. Edema of both legs appeared. There were anorexia and frequent bowel movements, accompanied by occasional incontinence of foul smelling fecal material. The blood smear showed immature white cells and the eosinophilia disappeared. She gradually failed, and died about four months after admission.

#### DIFFERENTIAL DIAGNOSIS

**DR. WILLIAM B. BREED:** This patient was on the ward when I came on service and was there when I went off. Practically everybody on the medical services at one time or another wrote words of wisdom about her and I hope I shall be permitted to read my own notes at this exercise. I have not learned what Dr. Mallory found, and so it was considered legitimate to modify the technic of these exercises a bit by allowing me to discuss a patient with whose clinical course I am familiar.

It appears from the record that this girl was sent into the hospital for study, probably with a question of rheumatic fever, rheumatoid arthritis or subacute bacterial endocarditis. I believe there was no definite diagnosis made before she was admitted. In the history of the present illness, rheumatic fever and rheumatoid arthritis are the two most likely diagnoses that are suggested. The physical examination brings up at once the question of subacute bacterial endocarditis. It is only when one learns that after she had been in the hospital for some time, evidence accumulated that a number of systems had become involved that one goes on to a more complicated diagnosis.

It is obvious that the liver and spleen were involved, and there are symptoms and signs suggestive of endocarditis. Scoliosis is mentioned but no abnormality in any of the joints. I can tell you that directly she was admitted she went slowly downhill and developed evidence of widespread systemic involvement characterized by bleeding from the mucous membranes, considerable anemia, pericarditis with effusion still further increase in the size of the liver and spleen and at one time, a rash on the arms and buttocks. Of course it seems impossible that this

whole picture could have been due to simple rheumatic fever or rheumatoid arthritis, and so with just a little reservation on rheumatic fever, —the malignant type,—I shall let both of these go

In discussing the laboratory work you will notice that she had persistent eosinophilia until the very last, which suggests at once two important diseases, namely, trichinosis and periarteritis nodosa. There was no history pointing to trichinosis. A biopsied piece of muscle was examined and found to have no cysts in it, and trichinosis is not a disease which will produce this whole picture. So the explanation of the eosinophilia rests rather strongly with periarteritis nodosa. She then developed this rash, which we had looked for quite often in the hope that we might be able to establish a diagnosis of acute disseminated lupus erythematosus, a syndrome that was very high on the list of possible diagnoses. The kidneys were functioning well. She had an increased sedimentation rate. She had an inverted albumin-globulin ratio. There was no evidence of parathyroid disease by chemical tests. Toward the end she had prolonged clotting and bleeding times. It is interesting that with this increase in clotting time the clot retraction and platelets were said to be normal, a fact which I think rules out a true purpura reasonably well. It is obvious that she had severe avitaminosis, and that brings up the question which is becoming so prominent today namely, How easily is the vitamin reserve depleted in a severe infection? I believe that the bleeding which occurred from the mouth and the accompanying local infection were caused by a depletion of vitamin C or K, or both, and not due to some fundamental blood dyscrasia. I just call attention to the statement "negative 17-ketosteroid determination", I take it that means the steroid was present in the urine and that she did not have adrenal disease.

DR. SEDGWICK MEAD Dr. Parsons tells me that there was a definite reduction of 17-ketosteroid.

DR. BREED A "negative" 17-ketosteroid determination does not mean anything. The fact that it was reduced suggests that the function of the adrenal glands was decreased in the presence of this infection, and that she did not have primary adrenal disease. Of course, the function of all the organs was decreased, and it is perfectly reasonable to expect that the function of the adrenal glands would also be lowered. She developed diarrhea and was proctoscoped, and no doubt the question of chronic ulcerative colitis was brought up. There was a glazed mucous membrane and the swabs showed blood, but there again I think

the colon took part in this generalized infection, and it is not legitimate to make a basic diagnosis of ulcerative colitis.

I should like someone to comment on the effect of the transfusions that this girl had, little appears in the record. At one time she was given fourteen transfusions in about as many days and showed a marked remission. The fact that she was returned to nearly normal health was due in our opinion to the repeated transfusions. After that she slumped again and I believe was given another series of transfusions.

DR. WYMAN RICHARDSON She was given many more.

DR. BREED Did she react as well to the second series as she did to the first?

DR. RICHARDSON No, although there was temporary slight response.

DR. BREED It is clear that only two diagnoses occurred to me as being important. These were acute disseminated lupus erythematosus and periarteritis nodosa. The appearance of the rash, although not typically distributed, and its disappearance with transfusion convinced me, as I left the case, that she was suffering from the former. I shall read what I wrote in the record: "Persistent eosinophilia, large liver and spleen, hematuria and other bleeding in the past, taken together with a negative lymph-node biopsy and a negative sternal bone marrow, leave periarteritis nodosa almost alone as a possibility. Suggest muscle biopsy."

Fourteen days later I wrote: "We cannot eliminate either lupus or periarteritis nodosa. The rash is not characteristic of lupus but lends some support to the diagnosis. Let us remember that often the pathologist cannot distinguish between these two syndromes."

DR. TRACY B. MALLORY I am going to challenge that statement, Dr. Breed.

DR. BREED Well, at least we have a challenge.

In casting about for other diagnoses, unusual to be sure, because this is an unusual case, I suppose one has to remember that she might have had tuberculosis. The fact that she responded rather remarkably to transfusion once and the fact that we never could make a diagnosis of tuberculosis while she was alive seem to make that quite unlikely. So I still am bound to rest on these two diagnoses, and I think now that if I had to put one before the other I should put lupus first and mention periarteritis nodosa, but not with any enthusiasm. I have no criticism to make of the treatment. I think she had about thirty transfusions—the only lead we had in the way of specific treatment in the hope that she might stage a more prolonged remission.

Dr. MALLORY As Dr. Breed has said, this patient was in the hospital several months and nearly everyone on the service saw her, a large proportion of them committed themselves to a note in the record. I might ask Dr. Richardson to express an opinion.

Dr. RICHARDSON I was on service when this patient died and I also made various diagnoses. She had during the last month of life an abnormal blood picture in that there were present quite numerous, very immature cells, some of them of the blast type. The blood picture, however, was quite suggestive of infectious mononucleosis. She did have a sore throat, and we went so far as to do a heterophile agglutination test, which was positive in a dilution of 1:64, as I remember it. However, I said at that time, "I think this patient has aleukemic leukemia or some leukemic-like disease", and I meant to include the possibility of lymphoma. We rather overlooked the bowel disease toward the end, although the diagnosis had been established by proctoscope.

After the patient died I kept the record out quite a long time before I put down the final diagnosis. I finally got tired of seeing the record around and wrote "No diagnosis as yet established. The patient died of hepatic failure and ulcerative disease of the colon."

Dr. BREED Do you know anything more about the bone marrow smear than you did then. There was considerable doubt apparently at that time.

Dr. MALLORY There was considerable difference of opinion about it. Dr. Jacobson, who did it, was inclined to think it did not rule out leukemia. I believe I saw it and did not think it was leukemia.

Dr. WALTER BAUER This patient would probably have died weeks before if she had not received such excellent treatment. Dr. Mead and the men on the service did an excellent job and deserve considerable credit.

I first saw this patient in consultation. She gave a history of a previous attack of arthritis of relatively short duration some two or three years before. At the time I saw her I was of the opinion that the joint signs, which were minimal, hepatomegaly, splenomegaly, generalized lymphadenopathy and eosinophilia could be explained on the basis of rheumatoid arthritis. Following her admission to the medical wards she became acutely ill, and it soon became obvious that we were dealing with a patient who was suffering from some disease other than rheumatoid arthritis. I was of the opinion that she was suffering from acute lupus erythematosus disseminatus and never had reason to change my diagnosis. The skin le-

sions over the mid-phalangeal and terminal joints were quite characteristic of those seen in disseminated lupus. I never was willing to accept the diagnosis of periarteritis nodosa. The only point in its favor was the eosinophilia. I should expect a patient with periarteritis nodosa as acutely ill as this girl was to have had symptoms referable to extensive vascular lesions, such as muscle cramps, cerebral accident or accidents, and signs of coronary heart disease. There is one other disease which could account for almost every symptom and sign presented by this girl, namely, an acute fulminating form of dermatomyositis. Such a diagnosis could explain the eosinophilia and all the other findings. However, she never exhibited facial edema, puffiness of the eyes or brawny induration of the skin and muscles. I did not see the autopsy. I was informed that she had a diseased colon. I am still of the opinion that acute lupus erythematosus disseminatus, plus superimposed deficiency disease with associated bleeding, would best explain the clinical picture presented by this patient.

Dr. MALLORY Would anyone else care to advance a diagnosis or second one of the nominations?

Dr. ALFRED KRANES It is very unusual for the liver and spleen and particularly the liver, to be as large as the one described here with either one of the two diagnoses put forth.

Dr. MALLORY We have not seen the liver markedly enlarged in any autopsy on lupus erythematosus.

A PHYSICIAN There is some evidence that she had amyloid disease due to chronic infection. That may account for it.

Dr. KRANES There was very little liver retention—only 66 per cent, probably not enough to establish a diagnosis of amyloid disease.

Dr. BAUER One of our cases with acute disseminated lupus erythematosus did show an enlarged liver with associated icterus of a mild grade.

Dr. MALLORY That was a dubious case.

Dr. RICHARDSON I hate the diagnosis of lupus. It is very vague—sometimes a medical waste basket. There is no definite pathologic picture. There is no check on it so far as I can see, and the tendency is to call every strange illness, lupus.

Dr. BAUER The situation as regards disseminated lupus is no different than that in many other disease syndromes which we encounter in medicine. I think we should consider it a definite disease syndrome and for the time being should continue to call it acute lupus erythematosus disseminatus.



DR RICHARDSON All right, but we should limit it to a very definite clinical picture

DR. BAUER All patients with disseminated lupus do not have a butterfly rash, nor do we expect to observe in any one case all the clinical findings characteristic of the disease. That would be expecting too much. I cannot agree with Dr Mallory's challenging Dr Breed's statement. I think the clinician has just as much right to a diagnosis based on clinical findings as has the pathologist who bases his diagnosis on histologic changes.

DR MALLORY What I was challenging was Dr Breed's use of the word "often." We had, it is true, one case\* in which confusion arose as to whether the diagnosis was lupus or periarteritis nodosa. So far as I know, however, it is unique.

DR BAUER I agree that the diagnosis of disseminated lupus must be made with care and considerable caution. We do not know the etiologic agent responsible for this disease syndrome. It may be that it is caused by one of a number of agents or by a combination of them. For the time being, however, we must continue to speak of it as a disease syndrome and continue to study each case in great detail if we are ever to learn more concerning it. I do not believe that Dr Mallory will find the widespread vascular changes ordinarily observed in periarteritis nodosa.

#### CLINICAL DIAGNOSES

Primary diagnosis not established  
Hepatic insufficiency  
Ulcerative colitis

#### DR BREED'S DIAGNOSIS

Acute disseminated lupus erythematosus?  
Periarteritis nodosa?  
(Secondary colitis and avitaminosis)

#### ANATOMICAL DIAGNOSES

Cirrhosis of the liver, with fatty infiltration  
Ulcerative colitis, acute and chronic  
Generalized lymphadenopathy  
Splenomegaly  
Pericardial effusion  
Hydrothorax, bilateral  
Acute disseminated lupus erythematosus?

#### PATHOLOGICAL DISCUSSION

DR MALLORY There is no question that the safest clinical diagnosis in this case is acute disseminated lupus because it is not possible for the pathologist to contradict that diagnosis. Nearly everything else that has been suggested I can contradict, and rule out quite definitely. We examined microscopically between fifty and sixty sec-

tions from this case and found no sign of vascular disease, so I think periarteritis is quite safely ruled out. The same can be said for dermatomyositis. We found no evidence of rheumatic heart disease, no evidence of rheumatoid arthritis. We did find several things that were quite unusual, and some of them were entirely unexpected. There was a very severe grade of ulcerative colitis. So far as the appearance of the bowel was concerned, I could not say it was not primary ulcerative colitis.

DR. BAUER Both grossly and on microscopic examination?

DR MALLORY Yes

There was a very large liver which was extremely pale and contained an enormous amount of fat, it was also finely granular, definitely and uniformly cirrhotic. The gross appearance was somewhat suggestive of an acute alcoholic cirrhosis in which one regularly sees large amounts of fat along with the cirrhotic process. However, we could not find any of the hyaline degeneration that is so uniformly present in acute alcoholic cases and is quite a reliable sign of this type of cirrhosis. Also, the appearance of the liver cells, the type of fat deposit, was not that of alcoholic cirrhosis. In such cases one usually finds fat globules of all sizes and a good many other evidences of acute progressive degeneration of the liver cells. Here the fat globules were uniformly large, and there were no signs of progressive liver-cell degeneration. Yet there was a definite cirrhosis. I can remember seeing only one similar liver, interestingly enough also in a case with ulcerative colitis and clinical evidence of multiple vitamin deficiency. Marked fat-infiltration of the liver is of course usual in ulcerative colitis but I have never seen cirrhosis except in these two cases.

The spleen weighed 800 or 900 gm, and I am inclined to think that the enlargement was mostly secondary to the cirrhosis of the liver. I do not believe it was a septic enlargement of the spleen but simply the result of a long-standing passive congestion.

There was a generalized lymphadenopathy, rather slight. The lymph nodes showed a marked toxic reaction in the germinal centers that is perfectly consistent with lupus erythematosus, but not distinctive of it. The bone marrow showed only hyperplasia, so leukemia is out. The kidneys were entirely negative, there was no suggestion of wire loop lesions. That, however, does not rule out lupus. There were also pleural, pericardial and abdominal effusions. They are characteristic of lupus but again far from pathognomonic. There was no amyloid deposit anywhere.

\*Case Records of the Massachusetts General Hospital. Case 24201. *New Eng J Med* 218:838-843, 1938.

I do not know what the correct diagnosis is. The immediate cause of death, I think, was unquestionably the combination of severe liver insufficiency and ulcerative colitis, but whether that was the primary or underlying disease or merely secondary complication, as the history suggests, cannot say.

Dr. KRAVES Do you still think it is possible that the patient had rheumatoid arthritis?

Dr. BAUER No

Dr. KRAVES Such patients occasionally have ulcerative colitis. One cannot fit the liver in, but the majority of the other symptoms can be.

Dr. BAUER I retracted my original diagnosis of rheumatoid arthritis a few weeks after the patient entered the medical wards. I remember one patient with ulcerative colitis who was seen in a number of Boston hospitals and diagnosed as a case of unexplained fever. At autopsy, however, he was found to have a very severe ulcerative colitis.

Dr. MALLORY Occasionally the diarrhea is not severe enough to be a primary complaint and may not be noticed.

Dr. BREED Dr. Richardson, did you write the discharge diagnoses?

Dr. RICHARDSON Yes hepatic failure and ulcerative colitis.

Dr. BREED Then you and Dr. Mallory win

Dr. RICHARDSON You could say that of Dr. Bauer about his lupus. I think there is not much question of winning. We all lose.

Dr. BAUER I wonder what the diagnosis in the *Journal* will be. You will have to commit your self.

Dr. MALLORY I have to make a guess, and my guess is going to be against lupus.

Dr. BAUER If you do not call it lupus, you cannot satisfactorily explain the symptoms which he experienced two or three years before or those present at the time of entry. Ordinarily, this is bad practice, and I believe it is to this case.

discomfort. He continued work and did not consult a physician until ten months before admission when the above symptoms, which had gradually increased in severity, suddenly became much worse, so that the pain appeared daily, caused him to double up, and radiated from the epigastrium through to the back. He had experienced no nausea, vomiting or change in the bowel habits. There had been no tarry or clay-colored stools. A physician prescribed a few "pills," which failed to bring relief. A few days later he entered an outside hospital, where he remained because of an "ulcer" that was demonstrated by x-ray. After one week's hospitalization, he was discharged on a milk-and-cracker diet, to which was later added chicken, eggs and fish. He improved with this diet, which he followed assiduously, but four months later epigastric pain began to recur. An occasional attack was so severe it caused him to roll on the floor. The pain required sedation by medication prescribed by his physician. One week before admission there was again a marked exacerbation of the symptoms, accompanied by nausea and vomiting of greenish, watery material but no "coffee-grounds" or gross blood. The bowels moved regularly once each or every other day but following the administration of a brown pill by his physician and a good dose of Epsom salts, the stools became black for several days. It was stated that the brown pill was an analgesic. Other associated symptoms during the present illness were anorexia, frequent belching of gas and the passage of flatus by rectum, an 18-pound weight loss during the five month period before admission, slight dyspnea on exertion and easy fatigability. The patient denied any mental or nervous excitement and stated that he used alcohol only occasionally. He smoked twenty cigarettes a day. Because of his symptoms he was admitted to this hospital for further diagnosis and treatment. The family mental and remaining past histories were non-contributory.

Physical examination revealed a thin but well developed man who was in no obvious distress. The teeth were dirty, carious and contained many fillings. Examination of the heart and lungs was negative. The blood pressure was 112 systolic, 80 diastolic. There was slight midepigastric pain on palpation of the abdomen but no muscular spasm or palpable mass was noted. The remainder of the examination was negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red-cell count of 4,700,000 with 75 per cent hemoglobin.

## CASE 26372

### PRESENTATION OF CASE

A fifty-one year-old Polish-born laborer was admitted to the hospital because of pain in the epigastrium.

Approximately four years before admission the patient noted the gradual onset of right upper quadrant and midline epigastric pain, which was sharp in character, periodic, and relieved by the ingestion of food. This pain occurred in attacks, usually at the close of the day and caused little real

and a white-cell count of 8100 with 67 per cent polymorphonuclears, the smear was normal. Examination of the urine was negative. Frequent stool examinations were negative for occult blood. A fasting gastric analysis showed a free acid of 31 units, and one half an hour after histamine a free acid of 112 units.

A gastrointestinal series performed in the Out Patient Department seven weeks previously showed a crater about 1 cm. in diameter on the lesser curvature of the stomach, at a point 3 cm. proximal to the pylorus. The surrounding rugae were thickened. The pylorus opened rapidly. The cap and the remaining duodenum were negative. There was normal filling of the upper loops of the jejunum. Another roentgen examination three weeks later showed no decrease in the size of the ulcer crater. There was marked thickening of the surrounding tissues, and the periphery of this thickening on the films appeared to be slightly lobulated. Six weeks following the first x-ray studies, after being on a modified Sippy regime and atropine, the ulcer had decreased in size. There was convergence of the rugae toward the ulcer. The surrounding swelling was still marked, unusually so for an ulcer that showed response to treatment. The swollen area appeared unusually rigid.

A gastroscopic examination was "probably unsuccessful," because the pylorus was not seen due to spasm of the antrum in the prepyloric region. The ulcer was not observed. Just distal to the angulus, on the lesser curvature, however, the mucosa showed a verrucous appearance, with increased reddening, indicative of hypertrophic gastritis. Elsewhere in the body of the stomach the mucosa appeared essentially normal.

Soon after admission an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR ALLEN G. BRAILEY. In the differential diagnosis in this case we must consider three possibilities. Did he have cancer of the stomach, did he have simply a benign ulcer, or did he also have some extragastric disease?

Let us weigh the possibility of cancer. First, he was forty-seven years of age when he first noted symptoms. The majority of patients with ulcer show symptoms before forty-seven. Also the majority of patients with cancer of the stomach usually are older than forty-seven. There are so many exceptions in either case that little help can be derived from the age. The record states that during the five months before admission he had lost 18 pounds. This is a large and rapid weight loss.

That symptom by itself points more strongly to cancer than to ulcer. Weight loss is not common in ulcer unless there is pyloric obstruction. In fact the frequent feedings which are taken to relieve distress often result in increased food intake and the patient may actually gain weight. X-ray examination showed no interference with stomach emptying. However, the report of nausea and vomiting suggests that he did develop at least functional obstruction at times. X-ray study presents an argument in favor of cancer in that the ulcer was close to the pylorus. We know that the closer an ulcer approaches to the pylorus the greater the possibility, indeed the likelihood, that it is carcinomatous. The x-ray film also showed marked thickening of the tissues around the ulcer, the whole area appearing rigid, a point in favor of cancer. Finally, the failure to be more than temporarily relieved by medical treatment is an argument on the side of cancer.

I think we should see the x-ray films, if we may.

DR AUBREY O. HAMPTON. These are the films taken at the first examination, the ulcer crater is here, and is within the prepyloric area. I think 3 cm. is perhaps a little exaggeration of the distance, but we shall not argue over a millimeter or two. The crater varies markedly in size, due to variations in filling. At examination a month and nine days later there is general reduction in the size of the lesion, at least it looks like a healing ulcer. I do not see any lobulation, and I am not impressed with the statement. I do see edema of the mucosa surrounding the ulcer, and not outcropping of tumor.

DR BRAILEY. The case for ulcer begins with the fact that he had had symptoms for four years. Most cases of cancer that have progressed to the point of causing pain result in a fatal issue within four years, but not necessarily so. The description of the pain is poor. I am not sure whether "periodic" means pain of a crampy character or whether it came on at the same time every day. It apparently was sharp and at times caused him to roll on the floor. That sounds more like gall-bladder or renal colic than the pain of ulcer. Yet such severe pain occasionally occurs with ulcer, and this makes it all the more difficult to distinguish it from the pain of cholecystitis. The fact that the pain was relieved by food is important and suggests irritability in the presence of gastritis with high acid, but food is apt to relieve any form of gastric disturbance to some extent. He was given a diet which helped him, but he went on smoking twenty cigarettes a day. I think this was a grievous error. There are few forms of digestive distress that are not made worse by smoking. Ulcers will often get well

even if smoking is continued, but I am sure the severity and duration of symptoms can be lessened by omitting tobacco.

Repeated stool examinations failed to show evidence of blood. I think it is true that benign ulcers are apt to bleed intermittently, whereas cancer of the stomach is rather prone to cause somewhat more continuous oozing.

He had a normal blood without evidence of anemia or infection. It is most important that his stomach showed an unusually high level of acidity. Such levels are reported in a small percentage of cancer cases, but much more frequently, of course, in benign ulcer.

Most gastric ulcers are not malignant, but all must be suspected of so being. The evidence as here given must be considered more in favor of benign than of malignant ulcer. This is another case in which the diagnosis is much less important than the decision as to treatment. There is no question but that he should have been operated on and probably should have had a gastric resection, regardless of the lesion found.

The history is vague and inadequate so that one should not be surprised if some unsuspected epigastric lesion were found, such as gall-bladder renal or possibly coronary disease, but I am not going to argue for anything else but benign ulcer.

Dr. EDWARD B. BENEDICT: Gastroscopic examination was unsatisfactory because of spasm of the entire antrum and prepyloric area. As to the chronic gastritis that we demonstrated and that was very severe, this is almost always an accompaniment of both gastric ulcer and gastric cancer and may occur without either. I do not believe we can say that the gastritis is in favor of ulcer or of cancer.

Dr. TRACY B. MALLORY: Dr. Hampton do you want to amplify your discussion?

Dr. HAMPTON: I believe he should have had his stomach resected. I think the chances of the ulcers being carcinomatous are very high even though it seemed to heal. We have seen healing of a malignant ulceration before in this hospital, especially in the prepyloric area. An ulcer may heal or appear to heal and still be malignant.

Dr. MALLORY: You base your argument on the location. I take it.

Dr. HAMPTON: Yes, otherwise it appears to be perfectly benign.

Dr. BENEDICT: I think it should be emphasized that any patient with a lesion as near the pylorus as that should be operated on.

#### CLINICAL DIAGNOSIS

Cancer of stomach?

#### DR. BRAILEY'S DIAGNOSIS

Benign ulcer of the stomach

#### ANATOMICAL DIAGNOSIS

Carcinoma of stomach: signet ring type.

#### PATHOLOGICAL DISCUSSION

Dr. MALLORY: This patient was operated on and a resection of the pyloric half of the stomach was done. The specimen showed two shallow ulcers with a little area of persistent mucosa between. One of these ulcers lay 1.5 cm from the pyloric ring—a little closer in the specimen than in the x-ray films. Its walls were very slightly indurated and it was not possible to be at all sure from palpation whether it was benign or malignant although the impression was slightly in favor of malignancy. Microscopic examination showed a signet ring carcinoma surrounding the areas of ulceration and also invading the wall of the stomach to the depth of a few millimeters. From the histological point of view there was no clear-cut picture of peptic ulceration. That does not rule out the possibility that the ulceration was peptic in character since the treatment in the last few weeks might have been effective enough to remove the customary histologic evidence.

Dr. HAMPTON: We were unable to find the second ulcer on these films. How deep was the smaller one?

Dr. MALLORY: About 2 or 3 mm.

Dr. HAMPTON: A centimeter from the pylorus?

Dr. MALLORY: Yes. This is, I think, the fifth case that we have seen in this hospital of an ulcerative lesion of the stomach which apparently decreased significantly in size in successive x-ray examinations under the influence of a medical regime for ulcer and which nevertheless was proved to be malignant on eventual histological examination. Hence, apparent, partial healing of an ulcerative lesion in the stomach with medical ulcer treatment does not rule out cancer particularly when it is in this area. In such cases there is no question that the conservative form of treatment is to resect, because you can never confidently rule out carcinoma.

Dr. MAURICE FREMONT-SMITH: Can you hazard any guess as to the length of time the neoplasm had been present? For four years?

Dr. MALLORY: I think it is quite possible. That is purely guesswork, but in other areas of the body that are more readily susceptible to examination than is the stomach we have become aware in the past ten years of non-invasive stages of carcinoma.

the atmosphere engendered by retreat and military failure. These items and others of the same category were found again and again in the preparation of the soil in which war neuroses grew. An advancing army, with an offensive objective, presents relatively few cases. A retreating army, with defeat and failure as its probable fate and defense as its objective, shows war neuroses in increasing numbers as the necessary hardships of a defeated army—insufficient rest, food and sleep—sharpen in proportion to the distance from the source of supplies and to the progressively disorganized contact with the bases of support.

As military protection decreases, the defenses of the human organism, primarily within that organism, begin to manifest themselves as individual responses without control, direction or inhibitions at conscious levels. These bizarre and varied clinical distortions represent the effect of fear and anxiety on the individual nervous, emotional and mental mechanism. A substitute for organized group effort in combative activities is thus supplied.

At Dunkirk, the atmosphere became individually and personally protective. Primitive self-conservation measures increased as the active phase of retreat became stabilized in inactivity. The dynamics and drive of active military participation crystallized in individual responses as the disorganized army was being hammered on all sides by destructive forces, against which no form of combative activity was possible. The passive hope for safety, in contrast to the inability to act, and the conflict so engendered released symptoms of nonpurposive and nonconstructive types in those soldiers who found it unconsciously expedient to act in this manner.

The authors point out a fact which the experience of World War I confirmed, namely, the soldiers who became victims of war neuroses were not, as a whole, different or distinguishable from those who did not. Excluding the obvious neurotics, which were only a small percentage of the whole, any soldier, given the essential conditions of a peculiar set of experiences and a characteristic situation, such as that at Dunkirk, may develop

the clinical picture of a war neurosis. The strongest personality when subjected to repetition of traumatic, daze-producing and terrifying incidents, in addition to the weakening experiences of hunger and fatigue, is not immune to neurotic reaction.

The average traumas in civilian life will produce neuroses in those whose hereditary trends, inherited constitutions or early experiences easily predispose them to the escapes and compromise maneuvers inherent in neurotic reactions. Even in civilian life, the unexpected, unusual and nonconforming experience, shot through with emotional tension, may turn a nervous system, hitherto controlled, into one untrammelled, and thus conditioned by neurotic explosions. This rare phenomenon in civilian life becomes a common pattern in the lives of soldiers exposed to the greater stresses of a situation such as that described at Dunkirk.

In World War I, the clinical description of the war neuroses was based on cases seen in base hospitals far from the combat areas, in rest camps or, oftenest, in more or less permanent refuges for the chronic cases. The acute neurosis developing at the combat areas showed much less pattern conformity than that described in this paper, and the selective, personal reaction type was much less frequent. The scope of the neuroses developed at Dunkirk was limited by the particular situation existing there. The personal neurotic response which replaced the general state of panic—fear, apprehension and anxiety—was an unconscious selection of that type of preservative reaction which was inherently determined by the individual victim.

In this series of cases, there are described the familiar clinical types—the crystallization of those symptoms which each individual uses as his personal formula for escape from a situation. The extraordinary dynamics of anxiety and fear made a more or less permanent pattern of the tremors of exhaustion. The physical recoils from explosions became the chronic reaction to minimal sounds. Similarly, respiratory increase to the panting stage, a reaction which is so characteristic of primitive and overwhelming fear, showed itself again when the initial experiences were suggested

by minor associations, by narrations of the retreat or by dreams and phantasies of happenings which, in some cases, were purely imaginative. The impulsive drive toward self-estimation and the necessity to intensify dramatically the worthwhileness of an experience and to explain the unmilitary conduct of a soldier, made the recounting of an incident largely a task of self justification.

If it is remembered that a good deal of this, and in many cases almost the whole of it, was carried out unconsciously and was tied to the primitive, fundamental and natural defense function of the nervous system as a whole, the clinical pictures seen from this article may be more readily understood.

Sargant and Slater show an understanding of war neuroses rare in the earlier war, and their treatment of these cases reflects this understanding very well. Rest, quiet, food and sleep are the primary therapeutic necessities. Sleep, however accomplished, is the outstanding necessity. The use of Sodium Amytal intravenously by the drop method ( $7\frac{1}{2}$  gr per day) is an unusual measure. This was done to render the patient more receptive to suggestion and exploration, persuasion and other psychotherapeutic measures. While this is an interesting addition to therapy and may have been necessary in the hospital setting where these cases were observed, it was thought not essential during World War I to depend so much on chemically produced suggestive receptivity because it was considered wise to rely as much as possible on the conscious individual response. One of the most difficult obstacles to cure in that war was the problem of return to active or sub-active service, where a repetition of the traumatic experiences was to be anticipated. The organization of neurotic symptoms as a defense against this was so therapeutically resistant that there was almost nothing remedial that could be done. This was particularly true of cases that had been hospitalized in England where a return to service implied transfer to France or other overseas activities. These problems do not exist at the present stage of this war, and therefore it would seem that intensive chemotherapy is not

required. The war neurosis-burdened soldier, returned to England becomes part of the insular defense system. He is on his own ground and must meet the defense requirements of a total population. From his neurosis may result a better use of his traumatic experience, and his self-estimation may be built up as a better solution to his problems than were his neurotic symptoms. It would seem that an active conscious therapy might be developed as a constructive antidote to a neurosis by taking advantage of the more positive horn of the conflict-dilemma, which is the traditional and customary conduct of a soldier, as opposed to the instinctive set of protective patterns linked to self-preservation.

It would be important and interesting to learn what the experience of the British Army fighting a defensive war on its own soil, might show in relation to the type, severity and permanence of the war neuroses, particularly in the case of soldiers who develop them in situations comparable to Dunkirk. A prophecy might be made that they would be less severe, less varied in type, less chronic and more general as expressions of fear, panic and anxiety also, less selective and less personal. This would be true because the atmosphere, though defensive as at Dunkirk, would have the stabilizing influence of plan and organized group security.

This paper of Sargant and Slater is a valuable and informative contribution to an old subject which is now brought back to notice in a new setting with a clearer insight into mechanisms than would have been possible without the experience of World War I.

## MEDICAL EPONYM

### DIETL'S CRISIS

Professor Joseph Dietl (1804-1878) of Cracow, Poland contributed an article entitled "Wandernde Nieren und deren Einklemmung [The Strangulation of Floating Kidneys]" to the *Wiener medizinische Wochenschrift* (14: 563-566, 579-581 and 593-595, 1864), from which the following translation is taken. He stressed the frequency of the occurrence of floating kidney, and outlined the physical findings. He reported nine case histories, in a

penter, Ph D, professor of biology, Tufts College, Wilfred M Copenhaver, Ph D, associate professor of anatomy, College of Physicians and Surgeons, Columbia University, Charles M Goss, M.D., professor of anatomy, University of Alabama Medical School, and Aura E Severinghaus, Ph D, associate professor of anatomy, College of Physicians and Surgeons, Columbia University Tenth edition 8°, cloth, 764 pp, with 448 illustrations Baltimore Williams & Wilkins Company, 1940 \$6 00

*Getting Ready to Be a Mother* By Carolyn Conant Van Blarcom, R.N. Revised by Hazel Corbin, R.N., general director, Maternity Center Association Fourth edition 12°, cloth, 190 pp, with 90 illustrations New York Macmillan Company, 1940 \$2.50

*The Rockefeller Foundation Annual report, 1939* 8°, paper, 507 pp New York Rockefeller Foundation, 1939

*The Mother's Manual for Family Control The fertile and sterile periods in a woman's life according to the Ogino-Knaus law of conception, Nature's way of controlling conception* 8°, paper, 13 pp, with 2 illustrations Cleveland, Ohio Health Calendar Company, 1937 25 cents

## BOOK REVIEWS

*Pulmonary Tuberculosis in Adults and Children* By James Alexander Miller, A.M., M.D., D.P.H., ScD., and Arvid Wallgren, M.D. 8°, cloth, 193 pp, with 43 illustrations and 20 tables New York Thomas Nelson and Sons, 1939 \$3.50

This book is based on two chapters by Drs Miller and Wallgren recently added to *Nelson's Loose Leaf Medicine*. Dr Miller deals with pulmonary tuberculosis in adults, while Dr Wallgren confines himself to tuberculosis in children. Since both authors appear to have written these chapters or sections independently, duplications and even differences of opinion are found. They both deal at length with the evolution of tuberculosis, as well as the roles of allergy and immunity. Many statements of Dr Wallgren definitely will not be accepted in this country, since his contribution is written entirely from the European point of view.

The section by Dr Wallgren deals mainly with his original researches at the Children's Hospital at Gothenburg, Sweden. One wishes that he could have given a résumé of the general present-day knowledge of tuberculosis in children rather than a discussion of that mainly derived from his own experiences. Tuberculosis has many problems which are of sectional character. What may be urgent in one country, may be of only secondary importance in another. Even in the United States many of the problems that arise in regard to the control of tuberculosis vary in each section of the country.

Discussing allergy and immunity, Dr Wallgren states that the rate of mortality among tuberculin positive children living with persons with an open tuberculous lesion is not higher than that among tuberculin positive children living in healthful surroundings. He further states that children who have successfully passed through an attack of primary tuberculosis are to be regarded as members of a picked group who, when exposed to tuberculous infection, are in a more favorable position than are uninfected children.

Dr Miller, dealing with the topic of danger of contact exposure, states that added infections hypersensitize the individual, producing a change in the heretofore latent lesions very similar to that of a tuberculin reaction, and

thus such lesions may be reactivated and eventually lead to phthisis. The recent work of Ch'iu, Myers and Stewart in Minnesota, and of Zacks, Sartwell and Pope, in Massachusetts, seems to bear out the same view.

Great progress has recently been made in the study of pathologic anatomy and the evolution of pulmonary tuberculosis. Both Dr Wallgren and Dr Miller deal with three stages in the evolution of phthisis. The first is that of the primary infection, the second is the phase of generalization, either by hematogenous or lymphatic channels, and the third is that of localization, and the only stage where collapse therapy may be applied.

The differential diagnosis and the clinical and roentgenological aspects are well treated. While Dr Wallgren devotes considerable space to treatment of tuberculosis, Dr Miller is rather brief, especially in dealing with the indications for collapse therapy and its complications.

It does not seem likely that the book will appeal to the undergraduate student or practitioner, nor is it exhaustive enough for the specialist. Undoubtedly, the authors would have taken more care in proportioning and coordinating their work if the writing of the book had been really planned by them.

*The First Five Years of Life A guide to the study of the preschool child* From the Yale Clinic of Child Development. Part I by Arnold Gesell, Ph.D., M.D., Part II by Henry M. Halverson, Ph.D., Helen Thompson, Ph.D., Frances L. Ilg, M.D., Burton M. Castner, Ph.D., and Louise Bates Ames, Ph.D., Part III by Arnold Gesell and Catherine S. Amatruda, M.D. 8°, cloth, 393 pp., with 21 plates New York Harper & Brothers, 1940 \$3.50

The authors have developed in this volume further consideration of the subject presented in an earlier volume, called *The Mental Growth of the Preschool Child*. The advances made in the understanding of the child since the earlier presentation make this new book particularly welcome. It goes without saying that anything written or sponsored by Dr Gesell is based on careful scientific observation and a long and varied experience in the study of the mental growth of children.

The book is concerned chiefly with the normal aspects of mental growth. It contains a description of the techniques used in the study of the preschool child. The changing character of the child is constantly emphasized. The authors point out that the preschool child is not a miniature school child but presents individual differences requiring study and evaluation. Emphasis is placed on the distinctive developmental needs and the hygiene of the early years of life. The preschool child is considered in relation to four basic fields of behavior: motor characteristics, adaptive behavior, language behavior and personal social behavior. The records are concerned with measurements taken at ten successive age levels: 4, 16, 28, 40, 52 and 80 weeks, and 2, 3, 4 and 5 years. A series of psychological portraits characterizing each age is thus obtained. All four of the basic fields are considered in relation to each age study. There are four chapters written by collaborators, these discuss chronologically the four basic fields throughout the period of the preschool child's development.

The volume presents a reliable source of information concerning the first five years of life. It will become a standard authority for anyone working in the field of mental growth, and a book of reference for all physicians having to do with the care of children.

# The New England Journal of Medicine

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VOLUME 22

SEPTEMBER 19, 1940

NUMBER 12

## MASSACHUSETTS MEDICAL SOCIETY

### Symposium on Syphilis\*

#### THE CLINICAL MANIFESTATIONS OF PRIMARY SYPHILIS

FRANCIS M. THURMON, M.D.†

BOSTON

THE clinical manifestations of primary syphilis are frequently deceptive and varied. They range from an insignificant lesion, so slight as to pass without notice, to multiple inoculation sites with as many as twenty chancres in a single case. Invariably, whatever type the initial lesion assumes, there is a perceptible enlargement of the regional lymph nodes. In women for example, with tertiary asymptomatic syphilis, approximately 40 per cent give no history and have no knowledge as to where, when or how they acquired their infection. Usually, however, careful history taking and physical and laboratory examinations, together with a detailed follow up of the family, reveal the approximate duration of the disease.

The typical Hunterian chancre, to the average physician is the characteristic initial lesion marking the onset of syphilis. In this connection we must not lose sight of the fact that this lesion, following a variable incubation period, requires from sixteen to twenty-one days to develop to clinical maturity. The local trauma created at the inoculation site is at first represented by a macule which develops into a papule. Local edema, lymphocytic and plasma cell infiltration, fibroblastic proliferation and eventually a peripheral obliterative endarteritis produce an eroded or ulcerative lesion, which in uncomplicated cases yields a serous exudate. The base of the erosion or ulcer is usually smooth while the border is continuous and regular. Genital lesions of this type in men are usually painless, but it is not uncommon for them to be painful when present as

an extragenital process or when involving the labia of a woman. The chancre may vary from one the size of a millet seed to an ulcerated tumor mass 10 cm in diameter, or a large plaque involving the entire labial or scrotal surface. In fact, a chancre may assume almost any conceivable morphologic form and may occur on any accessible skin or mucosal surface.

In these days of greater discussion of syphilis by the laity it is not uncommon to see patients at an early date following exposure. Often they present small denuded areas on the external genitalia which appear merely as superficial excoriations. A positive dark field examination in a lesion of this type is as definitely diagnostic as it would be on a typical Hunterian chancre.

The significant fact in all these cases is that the clinical appearance of the lesions alone is not diagnostic. Laboratory evidence, either as a positive dark field examination or as a positive serologic test for syphilis, or both, is necessary before an absolute or final diagnosis can be made, and certainly before treatment is instituted.

The pseudochancere redux which is a gummatous recurrence at the site of the original chancre, may simulate primary syphilis. The redux lesion however yields a negative dark-field examination seldom are the adjacent lymph nodes enlarged and usually there is a history of syphilitic infection in the past.

Resistant lesions of primary syphilis are occasionally encountered. I treated one lesion of this type on the penis which persisted with positive dark field examination after the patient had received a total of 5 gm of arsphenamine, several treatments with an insoluble bismuth compound and mercury and potassium iodide by mouth. The lesion was destroyed with radium. The patient re-

\*This clinical meeting was held and the following five papers read during the annual meeting of the Massachusetts Medical Society, Boston, January 22, 1940.

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covered from the syphilis in the usual fashion, in that he remained clinically asymptomatic and gave negative serologic reaction throughout the ten-year follow-up period.

Phagedenic genital lesions of syphilis are uncommon. Usually in these cases there is an accompanying Vincent infection, with large spiral organisms and fusiform bacilli which are of diagnostic significance.

The early lesions of lymphopathia venerea appear to be occurring more frequently in New England. These granulomatous lesions are not unlike those of early syphilis, but here the dark-field examination is negative, the Frei test is positive, and proper studies on the serum-albumin content of the blood are of diagnostic importance. Mixed infections occasionally occur. I have seen a case in which early syphilis, lymphopathia venerea and gonorrhea existed concomitantly in the same woman. To make matters worse, she also developed a sensitivity to bismuth and the trivalent arsenicals.

To diagnose a case as chancroid without completely excluding syphilis is an unsafe procedure. In approximately 54 per cent of infections of this type the two conditions are coexistent and syphilis is the major problem.

The possibility of meatus and hidden urethral chancres must not be overlooked. The conditions sometimes so closely resemble those of a non-specific urethritis that differential diagnosis presents a problem for the expert.

In view of the fact that so many cases of tertiary syphilis present no history of primary syphilis but give one of gonorrhea, it would seem justifiable to conduct an adequate serological follow-up for syphilis in all cases of gonorrhea.

Extragenital lesions are not uncommon. They occur with frequency on the lips, eyelids, nipples and anal region of both sexes. Digital primary lesions are sometimes encountered among physicians. There are cases in the records of the Boston Dispensary of infants, three months and six months of age, acquiring primary syphilis through an infected relative, who having no knowledge of infection kissed the infant on the eyelid and brow. In this connection, a lesion which is indurated, is slow to develop and heal and is associated with a marked satellite adenopathy should arouse suspicion of chancre until proof to the contrary has been obtained.

Digital lesions of specific origin have a tendency to form a painful granulating mass which does not clear with the usual application of antiseptics, lotions and ointments, rather, the lesion slowly and painfully increases in size and occa-

sionally presents a baffling problem. A lesion of this type is not unlike a melanotic whitlow. The importance of a dark-field examination in a persistent lesion of this type cannot be overemphasized.

Lip lesions of primary syphilis are frequently painful and swollen. I have clinical records of lesions of this type involving the upper lip and also the chin, which for weeks were treated with moist dressings, ointments and x-ray, on the assumption that they were carbuncles. In two such cases the secondary eruption had been mistakenly classified as dermatitis medicamentosa due to the use of sedatives.

The lip chancre may closely resemble a squamous cell epithelioma. Time-consuming diagnostic procedures in lesions of this type are not to be countenanced. The aid of an experienced observer in such cases is expedient. The presence of a repeatedly negative dark-field examination, together with a negative serologic test for syphilis on the blood, will rule out syphilis in 80 per cent of cases. With this evidence in hand, a frozen-section diagnosis, with the patient prepared for immediate operation, can be accomplished within the first few days of medical responsibility. Cancer and syphilis, especially tertiary syphilis, may exist in the same lesion, and cancer has the preference with regard to treatment.

The further differential diagnosis of lip lesions should include lymphogranuloma, avitaminosis, — chiefly of the vitamin B complex group, — pseudochancres, redux, inoculation tuberculosis, sarcoid, pyogenic granuloma, chancroid, blastomycosis and sporotrichosis.

Herpes of the lip deserves mention because occasionally a cluster of vesicles becomes confluent and superficial crusting develops. At this stage the lesion may resemble an early chancre of the lip. A herpetic lesion which requires more than two weeks for its involution should arouse suspicion of primary syphilis, especially if unilateral adenopathy has appeared. This applies also to a misdiagnosed, isolated, persistent impetigo-like lesion on the cheek or chin. The differential points here are recalcitrancy, lack of response to the usual treatment for impetigo and the complete absence of other impetiginous lesions, despite the fact that the signs may have persisted for two weeks or longer.

For lesions well inside the oral cavity or within the throat, a positive dark-field examination is not diagnostic. The reason is that normally there are spiral organisms inhabiting these regions which by dark-field examination are extremely difficult to differentiate from *Treponema pallidum*. They

are occasionally secondary invaders of lesions in the mouth or throat, the latter having an etiology entirely foreign to that of syphilis. I have seen such lesions in the throat, on the posterior half of the buccal mucosa or on the posterior two thirds of the tongue in nurses, social workers and physicians, which yielded positive" dark field ex-

aminations, but which cleared without treatment for syphilis. In these cases no further manifestations resembling syphilis occurred and serological follow-up through the succeeding year gave persistently negative results with the Hinton Wassermann and Kahn reactions.

520 Commonwealth Avenue

## THE INTERPRETATION AND RELIABILITY OF REPORTS OF SEROLOGICAL TESTS FOR SYPHILIS

TRACY B. MALLORY, M.D.\*

BOSTON

ACCIDENT has deprived you of the opportunity of listening to one of the foremost original contributors to the serological diagnosis of syphilis, and offers you instead a routine practitioner in the field whose major interests have been focused in other directions. I have nothing original to offer, and the data on which this paper is based are available to all, with minimal effort, in periodicals as widely distributed as the *Journal of the American Medical Association* and *Venereal Disease Information*. To those conversant with the field I can offer only a slight variation in emphasis and to the rest of you the saving of a few hours' time.

The greatest step in the serological diagnosis of syphilis since the discovery of the Wassermann reaction was unquestionably the development by Kahn<sup>1,2</sup> of a reliable and highly sensitive precipitin or flocculation test. Other precipitin tests had already been devised, but neither their sensitivity nor their specificity had been great enough to offer significant advantages over the standard Wassermann reaction. Any doubt that still existed regarding the superior sensitivity of the flocculation method was dispelled by the results of the international serological conferences staged under the auspices of the League of Nations from 1923 to 1930. Meanwhile other flocculation tests were developed, and some of the older ones were renovated in the light of newly discovered principles. It would be profitless to catalogue them. Four tests have emerged which have won wide acceptance in this country and which deserve discussion—the Kahn, the Kline,<sup>3</sup> the Hinton<sup>4</sup> and the Eagle.<sup>5</sup> In the meantime a slower and less advanced improvement in Wassermann-test technique has occurred and the methods of Kolmer<sup>6</sup> and Eagle<sup>7</sup> have won general attention.

The United States Public Health Service, in as-

sociation with the American Association of Clinical Pathologists has performed a most useful service in arranging a series of serological conferences in this country at which large numbers of blood specimens from known cases of syphilis and of control specimens from presumably non-syphilitic individuals have been submitted to the

TABLE 1 Sensitivity and False Positive Reactions Using Various Serological Tests for Syphilis (Second Conference)

TEST	SENSITIVITY	FALSE POSITIVE REACTIONS
	%	%
Kline	93.7	1.9
Kline (exclusion)	92.5	4.0
Hinton	91.3	0.0
Eagle (complement fixation)	87.7	0.0
Eagle (flocculation)	84.1	0.0
Kahn (presumptive)	82.2	1.0
Kahn	81.0	2.0
New York Sta. (complement fixation)	77.7	1.9
Kolmer (complement fixation)	59.5	0.0

expert serologists already mentioned, and also to other laboratories. The results have been extremely illuminating. In Table 1 are given some figures from the second conference.<sup>1-4</sup>

In any single series of this type the number of serums (approximately 300) is too small to justify statistical comparison. In successive conferences, moreover, both the sensitivity and the specificity of every test have varied within considerable limits. In Table 2 are listed the relative rankings in sensitivity and specificity in three successive conferences. In each of the paired series of figures the first number indicates the rank from the point of view of sensitivity, the second from that of specificity. The tendency to an inverse relation is obvious in the 1934 and 1937 figures. None of the 1938 tests showed any false-positive reactions.

It is apparent from these figures that there is no perfect serological test for syphilis. Both the sensitivity and the specificity of each test studied

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fluctuate within considerable overlapping ranges. Good flocculation tests should give from 80 to 90 per cent positive results in syphilitic serums, but as the upper limit is reached false-positive results begin to appear. Complement-fixation tests can be counted on for only 70 to 80 per cent sensitivity, but are somewhat less likely—provided they are properly performed—to produce false-positive results.

For those of you who practice in Massachusetts it is worth emphasizing that the Hinton test is at least as sensitive as any, probably the most sen-

TABLE 2 *Rankings of Various Serological Tests according to Specificity and False Positive Reactions (1934, 1937 and 1938 Conferences)*

TEST	RANKINGS		
	1934	1937*	1938
Hinton	1-6	3-0	1
Kline (exclusion)	2-7	2-8	2
Kahn (presumptive)	3-5	6-5	3
Eagle (flocculation)	4-4	5-0	7
Kahn	5-3	7-7	8
Kline	6-1	1-6	5
Kolmer (complement fixation)	7-2	8-0	4
Eagle (complement fixation)		4-0	6

\*A zero indicates no false positive reactions

sitive of all tests, and considering its extremely high sensitivity is remarkably specific. Crawford and Ray<sup>10</sup> have recently completed a survey of 21,000 Hinton tests performed in the Pathology Laboratory of the Massachusetts General Hospital. One hundred and forty-four cases showed positive reactions without confirmatory evidence of syphilis. In 90 of these, syphilis could be confidently excluded. The proportion of false-positive reactions, including all technical errors, lies somewhere between 0.4 and 0.7 per cent, if the 48 cases with patent technical errors are excluded it is almost exactly 0.5 per cent. If the Hinton test is consistently positive the chances that the patient has syphilis are at least two hundred to one.

Parran<sup>9</sup> has provided us some other figures which are well worth serious contemplation. The serological laboratories of all forty-eight states were invited to compete under similar conditions, checking their results against those of the expert serologists whose tests they were using. Thirty-nine accepted the challenge. A few of the results are shown in Table 3. It is all too evident that the variations between laboratory and laboratory are far greater than those between one test and another. Certainly Parran was not unduly stringent in his conclusion, "Some of the state laboratories are qualified neither to perform efficient laboratory service nor to inaugurate any system of state licensure or approval of local laboratories." Protagonists of compul-

sory premarital serological examination should study these figures. To the practitioner the moral is obvious. It is far more important to select carefully the laboratory to which you send your material than it is to worry about the particular test to be applied. As residents of Massachusetts we can feel proud that, due to the inventiveness and ability of Dr. William A. Hinton, our state laboratory was selected as one of the four yardsticks against which the achievements of the rest of the country were measured.

In the interpretation of serological tests for syphilis two premises must be constantly borne in mind. There are cases—or, perhaps better, stages—of progressive syphilitic infection in which one or another, or even all, the available serological tests are negative. There is no exclusion test for syphilis, although that name has unfortunately been applied to a modification of the Kline test.

Many of these negative reactions yet await explanation. Some may be definitely regarded as paradoxical, based on zone reactions. The content of antibody may be too great. In such cases dilution of the serum will produce a positive result. I have seen these zone reactions with the Hinton and the Kahn tests, and they have been reported<sup>11</sup> with the Wassermann and the Kline tests. The more sensitive the test, the greater is the likelihood of this reaction.

On the other hand, there occur with all known tests occasional false-positive results. Some of

TABLE 3 *Results of Serological Tests in Various State Laboratories*

TEST	LABORATORY	SENSITIVITY	FALSE
	No		POSITIVE REACTIONS
Kolmer		%	%
		88.0	0
	36	87.7	10.1
	8	55.0	0
Kahn	3	38.7	0
		84.5	0
	36	91.9	4.0
	33	95.9	9.1
Hinton	34	52.1	0
		92.9	0
	24	92.9	0
	14	81.0	0
Kline	32	46.7	1.0
		83.9	0
	2	65.6	0
	10	90.7	0
	30	88.8	3

these, even in the best of laboratories, must be classed as technical errors. They can usually be quickly identified because a single positive reaction is followed by a consistent string of negative ones. Others must be classed as true false-positive reactions since they persist over long periods of time.

They occur with predictable frequency in certain diseases—yaws, 100 per cent, leprosy, 50 per cent malaria, 10 per cent.<sup>12</sup> More important in Massachusetts is infectious mononucleosis. No figures covering the frequency of false-positive reactions in this disease are yet available, but every serologist has met a significant number of examples.

Other false-positive reactions appear without consistency, usually but not necessarily disappearing in a few days or weeks, in a great variety of conditions, such as streptococcal infections acute disseminated lupus and even chronic pulmonary tuberculosis.<sup>13</sup> Every positive serologic reaction unsupported by anamnestic or clinical evidence of syphilis demands frequent repetition, and preferably confirmation with another type of test.

With a multiplicity of tests discrepant results are certain. Schoch<sup>14</sup> reports that in Dallas, where five tests are used routinely, discrepancies appear in 25 per cent of the serums tested. How are these to be evaluated? Repeated examinations and careful and prolonged clinical correlation are the only available methods. Studies such as those of Crawford and Ray and of Schoch already quoted, and those of Stillman<sup>15</sup> are steadily increasing our knowledge. Where the Hinton or Kline test is positive and the Wassermann test negative the chances are two or three to one that the patient has syphilis. No blanket rule can be laid down, however, and each case must be carefully evaluated as an individual problem.

The serodiagnosis of syphilis is an expert's job. Adversers to the contrary notwithstanding, there exists no foolproof, instantaneous method suitable for individual testing in the doctor's office laboratory. Every short cut that has been attempted decreases both sensitivity and specificity. There is no possible way of adequately controlling the individual test, whereas in the large laboratory

variations in sensitivity rapidly become apparent if the percentage of positive results shifts significantly in one direction or the other.

### CONCLUSIONS

The serological diagnosis of syphilis has advanced greatly in the last fifteen years but there is still no perfect test for the disease. A negative reaction does not rule out and a positive one does not prove the presence of syphilis. The percentage of accurate diagnoses can be considerably increased by the use of multiple tests, but in the face of discrepant reports every case requires individual interpretation and the most exact clinical correlation.

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## THE DETECTION AND TREATMENT OF CARDIOVASCULAR SYPHILIS\*

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OF THE main types of heart disease, cardiovascular syphilis is the only one which is wholly preventable. Even when it is once established, early detection and proper treatment will stay its progress and prevent many of the serious complications. Nevertheless, this condition is responsible for more adult deaths than is neurosyphilis, and constitutes 10 to 15 per cent of all

cardiovascular disease. This deplorable situation is clearly not a consequence of meager available knowledge, but is rather to be ascribed to failure in detection and to inadequate treatment.

### DETECTION

From the clinical point of view, cardiovascular syphilis consists essentially of syphilitic aortitis with or without its three main complications, aneurysm, aortic regurgitation and narrowing of the ostia of the coronary arteries. The *Treponema*

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*pallidum* invades the thoracic aorta before or during the secondary stage of the disease, and inflammatory reaction continues to smolder for months or years, until sufficient damage has been created to give rise to clinical signs or symptoms.<sup>1</sup> The highest incidence of clinical manifestations occurs fifteen to twenty years after infection, but the interval may range from several months to fifty years. Almost all syphilitic patients show characteristic anatomic changes in the aorta at postmortem examination, whereas only 10 to 12 per cent have demonstrable clinical signs or symptoms. The diagnosis of syphilis consequently carries the implication that the aorta is or has been involved, even if clinical signs are not apparent.

By the time the diagnosis of cardiovascular syphilis can be based on frank clinical evidence, serious and often irreparable damage has already occurred. Any conspicuous reduction in the incidence of the disease depends primarily on the detection and adequate treatment of early syphilis in general, for cardiovascular syphilis occurs in less than 1 per cent of cases adequately treated early in the course of the disease.<sup>2, 3</sup> Thus in practically every case the clinical diagnosis of cardiovascular syphilis is evidence of previous neglect.

A consideration of the detection of cardiovascular syphilis comprises the detection of syphilis and of characteristic signs and symptoms of cardiovascular involvement.

In the detection of syphilis a negative serologic test does not preclude a positive diagnosis. From 20 to 30 per cent of patients with syphilitic aortitis or its complications have a negative serologic reaction. The diagnosis in these individuals must rest entirely on the history and physical examination. A history of syphilis or the description of an illness consistent with it must be sought by detailed direct questioning. The disclosure on physical examination of stigmas involving other organs raises a strong presumption in favor of the diagnosis.

The tendency of syphilitic infection to involve multiple parts of the body is reflected in the finding that from 50 to 60 per cent of untreated cases of syphilitic aortitis show evidence of neurosyphilis.<sup>4</sup> Conversely, at least 35 per cent of patients with neurosyphilis have been observed to show clinical evidences of cardiovascular syphilis.<sup>5</sup> If arsenic in the amounts usually employed in neurosyphilis is given to the latter group, the danger of cardiac damage is great.

The physical signs of cardiovascular syphilis are the signs of syphilitic aortitis, with or without its complications. The principal symptoms and signs

of uncomplicated syphilitic aortitis, recorded in the cases of the Co-operative Clinical Group<sup>6</sup> material, are as follows, in the order of their importance: teleroentgenographic and fluoroscopic evidence of aortic dilatation, a tympanitic, bell-like, tambour accentuation of the aortic second sound, a history of circulatory embarrassment, increased retromanubrial dullness, progressive cardiac failure, substernal pain, paroxysmal dyspnea, systolic aortic murmur and visibly or palpably increased pulsation in the episternal notch. Moore and his associates<sup>7</sup> believe that the presence of three or more of the first seven of these signs or symptoms in a patient with known late syphilis under fifty years of age is strong evidence for the diagnosis of uncomplicated syphilitic aortitis, and that the presence of any two of them renders the diagnosis probable.

Depending on the location and extent of the syphilitic process, the primary lesion of aortitis may be complicated by saccular aneurysm, aortic insufficiency or stenosis of the coronary ostia with resultant angina pectoris. Syphilitic myocarditis occurs but rarely. The suspicion of syphilitic involvement in any of the above conditions is strengthened if the onset is relatively abrupt, the past history of heart disease is negative, and the clinical course is rapidly progressive. Male patients predominate in the ratio of approximately 5:1.<sup>8</sup> To summarize, a positive diagnosis of cardiovascular syphilis can be made only when at least one of the following findings is present: a saccular aneurysm of the aorta or innominate artery, aortic regurgitation, appearing for the first time in a middle-aged person with a positive serologic reaction for syphilis, or a diffusely dilated aorta without aortic regurgitation or hypertension, past or present.

#### TREATMENT

The treatment of cardiovascular syphilis is aimed to relieve symptoms, prevent progression, and achieve gradual healing of the lesions. Reversal of the serologic reaction is not a primary objective. The earlier the stage of involvement, the greater the possibility of success. Thus, in uncomplicated syphilitic aortitis, adequate treatment has been observed to increase the average duration of life after detection from thirty-four to eighty-five months, whereas in aortic regurgitation the average duration was increased from forty months in the untreated to only fifty-five months in those receiving therapy.<sup>6</sup>

The former pessimism regarding the treatment of cardiovascular syphilis was due in part to the

sudden deaths or rapid deterioration which not infrequently followed vigorous arsenical therapy. The more favorable results of recent years have been attained by utilizing iodides and the heavy metals as the main basis of therapy.

The treatment of the patient with cardiovascular syphilis must consist in the first place of those measures, such as the regulation of activity and exercise, diet and other general hygienic measures, that have proved of value in the treatment of all heart disease. Particular attention must be directed to oral hygiene if the heavy metals are to be used. Congestive failure of even slight degree must be treated with prolonged bed rest before instituting specific therapy.

### Bismuth

While there is some difference of opinion regarding the various preparations of bismuth injected intramuscularly, the insoluble salts such as the subsalicylate suspended in oil have gained widespread adoption. Local reactions are mild, and if proper oral hygiene is practiced stomatitis causes but little difficulty. Renal damage must of course be avoided by weekly examination of the urine, but fortunately albuminuria and casts usually disappear rapidly on the reduction or omission of therapy. Initially, daily injections of 0.1 gm. of an oily suspension of bismuth salicylate every four or five days for four or five injections<sup>8</sup> are employed. If these are well tolerated, the dosage is increased to 0.2 gm. once a week for at least two or three months.

### Iodides

Iodides by mouth are given concomitantly, Moore and his associates<sup>9</sup> recommending 13 gm. of potassium iodide three times a day, with a rapid increase to as much as 12 gm. daily. Stokes and Anderson,<sup>10</sup> however, employ more moderate doses (0.3 to 0.6 gm.) three times a day.

### Arsenicals

Arsenicals are never administered until preliminary treatment with bismuth and iodides has been carried out for two to six months, and then only in small doses. Under no circumstances should severe reactions to treatment be risked, for considerable harm to the patient may result. The use of arsphenamine is contraindicated. Initial doses of 0.05 or 0.10 gm. of neoarsphenamine may be given, the dose being cautiously increased at weekly intervals to a maximum of 0.30 or even 0.45 gm. This course of treatment usually lasts ten or twelve weeks. At its conclusion iodides and injections of bismuth are again given and

the two methods of therapy are alternated for a minimum of two years. After that time long rest periods are permissible, but a course of bismuth and a course of neoarsphenamine are usually advisable once a year for the remainder of life. Bismarsen rather than neoarsphenamine has been utilized by Stokes, Miller and Beerman<sup>11</sup> in cases in which reactions had occurred or were expected. These authorities, as well as Moore and his associates,<sup>9</sup> find this preparation safe and effective. A final evaluation of the effectiveness of Mapharsen and of the recently introduced Sobisminol is not as yet possible.

The above schedule of treatment must of course be adapted to the requirements of the particular patient. Since, however, iodides and bismuth are well tolerated they may usually be given to patients with advanced cardiovascular lesions. If angina pectoris or aortic regurgitation exists or congestive failure has been present, arsenicals are to be given in small doses with extreme caution or to be omitted entirely, whereas in syphilitic aortitis, with or without sacular aneurysm the somewhat greater above-mentioned amounts may be utilized. In the management of these cases the governing basic principles have been well delineated by Stokes<sup>12</sup> and by Moore.<sup>13</sup>

Prolonged adequate treatment is necessary.

The value and danger of each drug must be clearly realized.

The patient must be questioned at each visit for symptoms or signs of toxicity.

The possible benefits must be carefully weighed against the possible dangers. Rapid healing of local lesions such as those about the root of the aorta is dangerous and the arsenicals if given too vigorously may lead to a Jarisch-Herxheimer reaction of "therapeutic paradox." Intensive therapy is borne more satisfactorily by young patients than by old patients.

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## THE EARLY CLINICAL AND LABORATORY MANIFESTATIONS OF SYPHILIS OF THE CENTRAL NERVOUS SYSTEM\*

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IT IS now well known that when the central nervous system is involved by syphilis this involvement takes place in the early stage of the infection. With the dissemination of the spirochetes at the time of the appearance of the secondary rash, the cerebrospinal fluid is infected.<sup>1</sup> The presence of the spirochetes in the central nervous system does not usually produce any symptoms except for a mild or moderately severe

The presence of abnormalities in the cerebrospinal fluid at the early stages does not necessarily mean that the patient will develop dementia paralytica or tabes dorsalis in the distant future since the fluid may become sterilized spontaneously or as the result of treatment in a small or large percentage of these patients, depending on the development of immunologic reactions and the amount of treatment received.

TABLE 1 *Frequency of Abnormalities in the Cerebrospinal Fluid in Early Syphilis*

AUTHOR	DESIGNATED STAGE OF DISEASE	NO OF CASES	CASES WITH ABNORMALITIES OF SPINAL FLUID	
				%
Cornaz <sup>4</sup>	Early	—	35	
Nicolau <sup>4</sup>	Early	51	35	
Bering <sup>4</sup>	Secondary	372	32	
Wile and Hasley <sup>4</sup>	Early	221	22	
Mills <sup>4</sup>	Primary	283	9	
	Secondary	768	35	
Zurhelle and Krehel <sup>4</sup>	Early secondary	113	16	
	Late secondary	31	48	

headache at the time of the rash, but abnormalities in the cerebrospinal fluid are quite frequent. The literature<sup>2</sup> since the report of Ravaut<sup>3</sup> in 1903 contains a large number of reports on the results of examination of the cerebrospinal fluid in the early stages of syphilis. The majority of the investigations report abnormalities in 25 to 40 per cent of the fluids removed after the appearance of the secondary rash (Table 1). The very significant conclusion which can be drawn from these studies is not that the cerebrospinal fluid may be involved in the early stages, but that when it remains normal for two or more years after the primary infection it will always remain so and parenchymatous neurosyphilis will never develop. The importance of this fact is obvious in that it permits the accurate forecasting of the possibility or probability of future serious symptomatic neurosyphilis and allows time for preventive therapy.

The degree to which abnormalities are present in the spinal fluid in the early stages is of some meaning in regard to the prognosis. Minor changes—slight increase in cells, slight increase in protein and a weakly positive Wassermann reaction—respond readily to treatment. On the other hand, when there is a pleocytosis, increased protein, an abnormal colloidal-gold curve and a strongly positive Wassermann reaction, intensive treatment is necessary to prevent the development of serious neurosyphilis.

In a study of patients in the latent period, that between the primary infection and the development of symptoms of the late manifestation of the disease, Moore<sup>5</sup> found that cerebrospinal fluid abnormalities were three times as frequent in patients who had received irregular treatment as in those whose treatment had been continuous, and that serious abnormalities were ten times as frequent in the irregularly treated group as in the group that had received good treatment.

From the above it is obvious that the central nervous system is frequently involved in the early stages of the infection. Clinical symptoms or signs of this involvement have always been uncommon, and they are now quite rare. This decrease in the frequency of clinical evidence is doubtless due to the more efficient treatment of early syphilis. The clinical symptoms in the early stages of the disease are the result of involvement of the meninges or the blood vessels. These may occur separately or there may be a mixture of both in the same individual. The symptoms may be confined to the brain or to the spinal cord.

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## SYPHILITIC MENINGITIS

Syphilitic meningitis<sup>6</sup> usually develops within the first six months of the infection, and the signs and symptoms of the inflammation of the meninges may be present along with the secondary rash. It was argued for some time that the appearance of syphilitic meningitis was due to treatment with arsenic, the theory being that the arsenic had driven the spirochetes into the nervous system and caused the meningitis. This hypothesis is, of course, without foundation, and probably arose from the fact that the introduction of arsenic in the treatment of syphilis was coincidental with the development of the technique of removing and examining the cerebrospinal fluid. In the vast majority of cases the meningitis develops in patients who have received no previous treatment or an amount that was entirely inadequate. A common story is for the patient to report to the doctor with a primary lesion and receive three to six injections of an arsenical, and allow the treatment to lapse. After an interval of six to twelve weeks, he begins to complain of headache, nausea and vomiting and cranial-nerve paralyses appear. He is thereupon admitted to the hospital with the full-blown clinical syndrome of syphilitic meningitis and the typical cerebrospinal fluid abnormalities.

Syphilitic meningitis is a relatively rare complication of syphilis occurring in less than 0.5 per cent of the cases, and since emphasis has been placed on the value of arsenic in the treatment of early syphilis, the condition is now a clinical rarity. I have never seen it develop in a patient while receiving regular treatment with one of the arsenicals, but it was not an uncommon experience for the symptoms to have their onset while the patient was supposedly taking mercury rubs at home.

Patients with syphilitic meningitis of the brain may be divided into three groups, according to whether symptoms are present indicating selective involvement of the meninges at the base or over the convexity of the brain. The first group (acute syphilitic hydrocephalus<sup>6</sup>) comprises those cases without evidence of any selective involvement. The signs and symptoms include headache, nausea, vomiting, choked disk, stiffness of the neck, and abnormalities in the cerebrospinal fluid. The symptomatology is due to an excess formation of cerebrospinal fluid and an impairment of the absorption of the fluid resulting from the inflammatory reaction. The following case is a typical example.

Case 1. M. P., a 24-year-old woman, was admitted to the hospital in March 1933 with complaints of headache, weakness, vomiting and blurring of vision for 3 weeks.

In May 1932 she had had a secondary rash and was given nine intravenous injections of neosalvarsan and ten intramuscular injections of bismuth. She was nauseated and vomited after the intravenous injections and did not return for treatment after December 1932.

On examination there was stiffness of the neck, choked disks and generalized hyperreflexia. The blood Kahn test was positive. The cerebrospinal fluid was under pressure of 300 mm. of water; it contained 250 lymphocytes and 35 polymorphonuclear leukocytes per cubic millimeter and 59 mg of protein per 100 cc., the colloidal gold curve was 0012223210 and the Wassermann reaction was positive. The cerebrospinal fluid pressure was controlled by lumbar punctures and the patient was given injections of neosalvarsan and bismuth. After 3 weeks she was discharged improved. Treatment was continued in the Out Patient Department and after 1 year she was symptom free. The blood Kahn test was negative and the cerebrospinal fluid was entirely normal.

In the second group (basilar meningitis) the inflammatory process is concentrated around the base of the brain and in addition to the general symptomatology of increased intracranial pressure

TABLE 2. Relative Frequency of Involvement of the Various Cranial Nerves in Syphilitic Meningitis<sup>6</sup>

CRANIAL NERVE	INVOLVEMENT %
I	1.5
II	26.0
III	23.0
IV	2.5
V	11.0
VI	21.0
VII	40.0
VIII	41.0
IX, X	6.0
XI	0.5
XII	3.5

there occur the symptoms due to involvement of the various cranial nerves. The nerves around the cerebellopontine angle (sixth, seventh and eighth) are most frequently affected and those in the interpeduncular space (second and third) come next (Table 2). The following case is illustrative.

Case 2. N. A., a 22-year-old housewife, was admitted to the hospital in November 1930 complaining of headache, dizziness, tinnitus and slight loss of hearing in the right ear and paralysis of the right side of the face of 7 weeks duration. In July 1930 she had had a secondary rash and received four injections of neosalvarsan.

On examination there was horizontal nystagmus, slight impairment of hearing in the right ear, paralysis of the right 7th nerve and weakness of the right 6th and left 7th nerves. The deep reflexes were hyperactive. The blood Kahn test was negative. The cerebrospinal fluid pressure was normal; the fluid contained 340 cells per cubic millimeter and 73 mg of protein per 100 cc., the colloidal gold curve was 4333333322 and the Wassermann reaction was positive. The patient was treated with neosalvarsan, Tryparsamide and bismuth with rapid improvement of symptoms, and at the end of 18 months of treatment she was symptom-free and the cerebrospinal fluid was entirely normal.



The third group of cases (vertical meningitis) are those in which the meningeal involvement is concentrated over the convexity of the brain. These patients show, in addition to the signs of increased intracranial pressure, mental symptoms, confusion and convulsive attacks, and it is in this group that vascular lesions with transient or permanent hemiplegias are commonest. The following case is typical.

CASE 3 M J, a 33-year-old salesman, was admitted to the hospital in 1931 with the complaint of headaches and three minor convulsive attacks in the last 3 months. He had had a small penile lesion 1 year previously, which disappeared without treatment. The neurological examination was not significant. The blood Wassermann test was positive. The cerebrospinal fluid was under pressure of 200 mm, it contained 117 white cells per cubic millimeter and 192 mg of protein per 100 cc, the colloidal-gold curve was 0001222222 and the Wassermann reaction was positive. The patient was treated with neosalvarsan, Tryparsamide and bismuth, with complete relief from symptoms. The blood Wassermann test was negative and the cerebrospinal fluid was entirely normal after 15 months of treatment.

A patient with syphilitic meningitis should be hospitalized and treated intensively with one of the arsenicals and one of the heavy metals. The cerebrospinal-fluid pressure can be controlled by spinal punctures at appropriate intervals. The arsenical should be administered in proper doses at four- to six-day intervals, together with the heavy metal intramuscularly and iodides by mouth. Under this regime the symptoms rapidly disappear, the cerebrospinal fluid pressure falls to normal and the swelling of the optic disks

TABLE 3 *Effect of Treatment in the Ultimate Outcome in Syphilitic Meningitis<sup>5</sup>*

TYPE OF TREATMENT	ULTIMATE OUTCOME	
	GOOD	POOR
Adequate	%	%
Poor	86	14
	33	67

subsides. Two or three weeks in the hospital is generally sufficient to restore the patient to nearly normal. Complete recovery of paralyzed cranial nerves may require more time, and it is unusual for complete recovery to result when the eighth nerves have been affected. This is explained by the fact that the paralysis of the eighth nerve may not be due to the meningitis alone, but also to the concomitant lesions in the nutrient artery of the nerve. The important fact to be borne in mind in all cases of syphilitic meningitis is that treatment must be continued for at least eighteen months. Alternating series of one of the arsenicals and one of the heavy metals should be given,

with control of the cerebrospinal fluid at intervals of six months. The treatment should be continued until the cerebrospinal fluid is entirely normal and for at least eighteen months, even though the fluid becomes normal before this time. With continuous treatment until the fluid is normal, the prognosis is excellent and future parenchymatous neurosyphilis should not develop. But if adequate treatment is not given, the possibility of more serious latent syphilis of the nervous system is great<sup>5</sup> (Table 3).

EARLY VASCULAR NEUROSYPHILIS

*Cerebral Lesions*

The blood vessels of the brain may be involved early in the course of syphilis, but the occurrence of vascular accidents in the first few years of the disease is rare. The vascular lesions in early neurosyphilis are usually accompanied by a moderate or severe degree of meningeal reaction, in contrast to those which occur late in the disease, where the meningeal element may be almost or entirely lacking. The symptoms of early vascular syphilis of the brain are those of vascular disease in general. Since meningitis is usually a concomitant factor, many of these patients complain of headaches for several days or weeks before the onset of the vascular insult. With thrombosis—the lesion that produces symptoms—there may be convulsions, coma and neurologic residuals, depending on the site of the vessel thrombosed. Since the middle cerebral artery is the one most commonly involved, the symptoms are usually those of a hemiplegia or a hemianesthesia. Other neurologic syndromes such as aphasia, hemianopia and those due to lesions of the brain stem also may result from vascular occlusions in early syphilis of the blood vessels. The treatment is essentially similar to that outlined for meningeal neurosyphilis. The prognosis in regard to life is good, since these lesions are rarely fatal, but that in regard to return of function of disabled members is more complicated, and is dependent chiefly on the size of the vessel thrombosed and on whether this vessel actually nourished a vital area. Treatment is directed mainly toward the prevention of future vascular lesions or parenchymatous neurosyphilis. The treatment itself cannot be expected to affect the softening of the brain that has resulted from the vascular occlusion.

The following cases illustrate different types of cerebral lesions. In Case 4, there was early cerebral vascular neurosyphilis with a marked degree of meningitis, and in Case 5, early meningeal and vascular syphilis of the cord was followed by cerebral lesions.

**CASE 4** T. H., a 30-year-old sailor was admitted to the hospital in 1933 with a right hemiplegia which had developed during sleep the night before. He had complained of headaches for the last few weeks. On examination there was a generalized secondary rash and a right hemiplegia involving the face and the right arm and leg. The blood Kahn test was positive. The cerebrospinal fluid contained 700 lymphocytes per cubic millimeter, the colloidal-gold curve 1112222210 and the Wassermann reaction positive. The patient was treated with neosalvarsan and bismuth. The hemiplegia improved rapidly and he was discharged, with instructions to return to the Out-Patient Department for further treatment.

**CASE 5** C. McD., a 26-year-old laborer was admitted to the hospital on June 14 1929 complaining of difficulty in walking. Three and a half months previously he had had a penile chancre, which was followed by a secondary rash and iritis. Six days before entry there was numbness and weakness of the legs which increased in severity.

On examination there was a fading secondary rash, generalized adenopathy and acute iritis. There was a spastic weakness of both legs, with knee and ankle clonus and bilateral Babinski reflexes. Sensation was well preserved. The blood Kahn test was positive. The cerebrospinal fluid was under normal pressure. It contained 80 white cells per cubic millimeter and 120 mg. of protein per 100 cc. the colloidal-gold curve was 1112222210 and the Wassermann reaction was positive. The patient was given seven injections of arsphenamine, 0.4 gm. each, with rapid improvement in the strength of the legs, and was discharged on July 19 to receive further treatment in the Out-Patient Department. He visited the department only four times in the next 9 months and was readmitted to the hospital on April 25 1930 with a paralysis of the left arm and leg which had developed suddenly the day before entry. The cerebrospinal fluid contained 80 white cells per cubic millimeter and 105 mg. of protein per 100 cc. the colloidal-gold curve was 4443333210 and the Wassermann reaction was positive in 0.1 cc. of fluid. He remained in the hospital 1 week, during which time the hemiplegia rapidly improved. He received continuous treatment in the Out-Patient Department for the next 2½ years with neosalvarsan, Tryparsamide and bismuth. At the end of this time he was symptom-free and examination was negative except for hyperactive reflexes in the legs and a slight diminution of vibratory sense in the tibia. The blood Hinton test remained positive but the cerebrospinal fluid was entirely normal.

### Spinal Lesions

In early neurosyphilis of the spinal cord there is usually an admixture of meningeal and vascular involvement (meningomyelitis). When the meningeal involvement predominates the symptoms are those of a mild spinal myelitis, with stiffness of the legs, weakness, hyperactive reflexes and the Babinski sign (Case 5). With extension of the involvement to the blood vessels the lesions in the cord are much more extensive and there may be a complete transverse myelitis with a flaccid paraplegia, complete loss of sensation and areflexia (Case 6). The signs of meningeal involvement usually precede those of vascular disease, and if treatment is initiated at this stage, progress of the

disease to the blood vessels can usually, but not always, be prevented. When the weakness is accompanied by spasticity the results of treatment are usually quite encouraging, but once a flaccid paralysis with complete loss of sensation has developed there is little chance of any return of function in the legs, and death often ensues from the development of bed sores or ascending urinary infection. The following case is one of early syphilitic meningomyelitis, with thrombosis of the spinal vessels.

**CASE 6** M. F., a 45-year-old man, was admitted to the hospital on February 11 1929 with complete paralysis of both lower extremities of 6 days' duration. Twelve months previously he had had a chancre on the index finger and 10 months previously a generalized rash and sore throat. Three months before entry there had been a transient weakness of the legs which left him with a limp and with imperfect control of urination.

On examination there was a flaccid paraplegia with complete anesthesia below the 4th lumbar segment and hypesthesia below the level of the 6th dorsal segment. There was rectal and vesical incontinence. The ankle jerks were absent, and the knee jerks were feeble. The blood Kahn test was positive. The cerebrospinal fluid was under normal pressure. It contained 108 white cells per cubic millimeter and 129 mg. of protein per 100 cc. the colloidal-gold curve was 5555432110 and the Wassermann reaction was positive. The patient remained in the hospital for 6 weeks, during which time he was treated intensively with neosalvarsan iodides and mercury. There was no improvement in the paralysis or sensory loss. He developed an extensive decubitus and died of septicemia.

### SUMMARY

Laboratory evidence of involvement of the central nervous system can be found in approximately 40 per cent of the patients with untreated syphilis if the cerebrospinal fluid is examined in the first few months following the appearance of the secondary rash. Clinical symptoms or signs of this involvement are rare, and the significance of the abnormalities in the fluid at this stage lies in the fact that they indicate that serious late syphilis of the nervous system—dementia paralytica or tabes dorsalis—is apt to develop unless proper treatment is given. For this reason the cerebrospinal fluid should be examined in all patients with syphilis. It has been recommended<sup>4</sup> that a patient undergoing treatment for early syphilis should have an examination of the cerebrospinal fluid after six months of treatment and again at about eighteen months, or on completion of treatment. It is not always practicable to puncture the patient twice, and in such cases the puncture should be performed at the latter time. No patient should be discharged from treatment as cured until the cerebrospinal fluid has been examined.

and found to be entirely normal regardless of the results of the serologic tests on the blood

The treatment of patients with asymptomatic or symptomatic involvement of the nervous system in early syphilis is essentially the same as that for early syphilis in general, namely, trivalent arsenicals, bismuth or mercury, and iodides. Treatment must be continued, however, until the cerebrospinal fluid is entirely normal. If this is not accomplished by eighteen months to two years of routine treatment, the further treatment should be

modified to include the use of Tryparsamide and, if necessary, artificial-fever therapy

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## THE PUBLIC-HEALTH ASPECTS OF SYPHILIS AS IT CONCERNS THE GENERAL PRACTITIONER

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FOR nearly fifty years Massachusetts has been a leader among the states in recognizing the venereal diseases as a problem of public health. Legislation in regard to venereal disease in Massachusetts dates back to 1894. The first state-supported Wassermann laboratory opened here in 1915. In 1918 Massachusetts became the first state to supply arsphenamine free to physicians, clinics and institutions treating syphilis.

During the current nationwide program for the control of venereal disease this commonwealth is again in the front ranks. For the fiscal year 1940 Massachusetts has available for venereal-disease control from all sources 10.2 cents per capita, of which state and local appropriations amount to 7.7 cents. This is about 3 cents more than the average per capita state and local contribution for the country as a whole.

Confidently we can affirm that Massachusetts' newly enacted prenatal law will tend to reduce congenital syphilis to the vanishing point. Through twenty years of relentless war against syphilis, the English have pushed down their rate of infant mortality due to this disease from 20 per 10,000 live births in 1917 to 2 per 10,000 in 1938<sup>1</sup>. Even indirect control measures such as a premarital-blood-test law has an immediate effect measured in declining congenital syphilis rates. For example, the premarital law of your good neighbor, Connecticut, has been on the books for only four years. Yet in thirty-six months the number of reported cases of congenital syphilis in infants has dropped from 38 in 1936 to 16 in 1938—and only 7 cases were reported for the first six months

of 1939<sup>2</sup>. Yes, congenital syphilis disappears before determined attack.

The already excellent serological laboratories of Massachusetts are constantly striving for higher efficiency. Well-trained epidemiologists and follow-up workers are available to each of you through the State Department of Health.

But state action alone—no matter how abundant or necessary—cannot wipe out syphilis. This is not a problem of catching rats or testing water. This is a human problem. Finding and treating syphilis strike at the intimate life of the individual. The patient immediately raises natural and artificial barriers—the physician alone is capable of breaking through them.

However, before we consider what the practitioner can do for the control of venereal disease, let us think briefly about what such control may mean to the practitioner. About four years ago a survey was conducted by the United States Public Health Service in Richmond, Virginia, concerning the economic factors underlying the control of syphilis<sup>3</sup>. At that time nearly one third of all private patients with venereal disease were being treated by private physicians with little hope of remuneration. Although many of these patients could afford to pay—and did pay—for most of their medical requirements, the extended treatment for syphilis was beyond their means. From any viewpoint, such an arrangement is unfair to the physician. Why should his services be demanded for public charges without compensation? Regardless of good intentions, the relatively small body of physicians cannot shoulder a responsibility that rightfully belongs to society as a whole. With a well-equipped, tax-supported clinic at hand this

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concentrated burden is lifted from the physician. Ample experience indicates that the public venereal disease clinic is the economical method of treating the patient who cannot afford private care.

Unfortunately, the economic status of the individual is invariably reflected in the economic status of the community. Communities in which a large proportion of individuals cannot afford treatment for syphilis are themselves unable to afford adequate medical care for these individuals. It is doubtless true that poor communities need health services more than do the wealthy. Congress has kept this in mind when directing that federal funds for venereal-disease control shall be provided on the basis of financial need as well as upon extent of the problem.

For example, it is estimated that over 60 per cent of all persons infected with venereal disease in the United States are concentrated in seventeen Southern states, which have the lowest per capita income. From the standpoint of venereal-disease control, it is highly significant that these same states contribute most to the rising stream of interstate migration. The problem of venereal-disease control cannot be isolated to a particular geographic region. It is a problem for the nation and must be attacked on a nationwide basis. Some areas—Massachusetts is such an area—are capable of conducting an adequate local control program. Other areas require outside help.

The establishment of clinics providing part pay or free treatment for indigents is attended of course, by many dangers. Recently there was brought to my attention a confidential report prepared by a medical man highly respected in his own community, in which he points out the dangers which arise when the county medical society exclusively dictates how, by whom and to whom clinic care is to be given. This policy reaches the heights of absurdity, he states, in one area where fourteen local physicians, largely older men, wish to serve in the clinic, presumably for the small financial return. They rotate in service, each attending the clinic for two weeks at a time.

How can there be uniformity of service under such conditions? None of these physicians are trained; some will never be able to master the techniques of treatment, and no one of them has that responsibility for overseeing the whole which will enable him to develop and enlarge the service. This is not venereal-disease control, but it does tend to discredit the vast majority of physicians who are trying to make such control a reality.

It has been argued that such experience makes better physicians of these doctors, in their private practice. In my opinion, a public clinic is estab-

lished to provide adequate and economical diagnosis and treatment to a section of the population unable to provide for themselves. While it is available for observation and training, it is not primarily an educational institution. I am happy to see that you in Massachusetts are approaching the problem of physician-training in the treatment and control of venereal disease in a more effective manner—through a training program jointly sponsored by the Massachusetts Medical Society and the Massachusetts Department of Public Health.

On two occasions, during the spring of 1937 and the corresponding months of 1939, surveys were conducted to determine the constant syphilis-treatment load in Chicago. All clinics and all but twenty of six thousand Chicago physicians participated. In the intervening two years, an extensive venereal-disease educational program had been begun. At the time of the second survey, the early syphilis-treatment load in the clinic increased about one third. This load among private practitioners had increased by an almost identical percentage.\* Present-day education seems to have brought new cases to the physician from the middle income group—a group able to purchase most of its medical care.

Education not only tends to bring more infected persons under treatment; it also helps the physician in case holding. It shifts the burden of proof from him in making a diagnosis. It makes the prenatal blood test easier to take. It permits him to include examination for venereal disease as a routine part of his clinical procedure.

Well-organized syphilis control implies good epidemiology and follow-up service. When the program provides it, the practitioner can make good use of case follow-up. For example, the State of Illinois has a trained venereal disease follow-up staff.\* In 1939 private physicians reported 937 delinquent patients to the venereal-disease control officer, of these 552 (59 per cent) were returned to treatment. The same physicians reported 878 suspected contacts by name, of these, 331 (38 per cent) were located, examined, found infected and placed under treatment. In 2486 contact investigations started on newly reported cases, treating physicians failed to co-operate with the state investigator in only 92 cases. This is a remarkable tribute to co-operative effort. Illinois physicians have found that an intelligent investigating service is worth while. When both the state and the physician share the responsibility, syphilis control becomes a reality.

Despite its doubtful reputation, we know that syphilis is not confined altogether to the poor and criminal classes; yet we may hesitate to suspect an

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## NON-SURGICAL CONDITIONS SIMULATING ACUTE APPENDICITIS IN CHILDREN\*

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THERE are many nonsurgical conditions that closely simulate acute appendicitis in children. In this paper 9 of the more interesting cases of this sort that have recently been observed at the Children's Hospital are presented. In each case some member of the surgical staff seriously entertained the diagnosis of appendicitis, in a few, operation was actually performed. But in all cases the cause of the symptoms, in the broadest sense, lay outside of the peritoneal cavity.

There is an equally interesting group of cases representing surgical conditions simulating appendicitis<sup>1, 2</sup>, but since these, like appendicitis, require operative treatment, and as their differential diagnosis has been frequently emphasized, they will not be discussed here. Discussion of such familiar differential considerations as mesenteric adenitis, pyelonephritis, gastroenteritis and chronic constipation is likewise omitted.

The following list represents the correct diagnoses for the cases under discussion. Typhoid fever, measles, migraine, diabetic acidosis, allergic gastroenteritis, rheumatic fever, lobar pneumonia, sickle-cell anemia and leukemia.

### CASE REPORTS

CASE 1 R. S., a 7-year-old Negro, was admitted to the Medical Service of the Children's Hospital on June 26, 1939, because of fever and abdominal pain of 7 days' duration. He was constipated and had not vomited. The pain at first had been umbilical, but for the 48 hours before entry it had been localized in the right lower quadrant. The temperature was 102°F and the pulse 128. Physical examination showed localized tenderness and involuntary spasm in the right lower quadrant, with some less marked, generalized abdominal tenderness. Rectal examination showed tenderness on the right. The urine and stool examinations were normal. There was no evidence of shock or loss of blood. The white-cell count was 7400, with 73 per cent polymorphonuclears. Surgical consultants on the night of admission found the same physical signs, and after careful consideration decided that the possibility of an acute appendix was great enough to

warrant exploration. As the operating room was being prepared, a positive Widal test was reported. Operation was postponed. The Widal test was verified, and *Eberthella typhosa* was cultured from the blood. The subsequent course was that of satisfactorily treated typhoid fever.

CASE 2. R. H., a 7-year-old boy, was admitted to the Children's Hospital on July 1, 1935, because of abdominal pain and nausea of 48 hours' duration. The pain was intermittent and was localized near the umbilicus. The day of admission he vomited. Three years previously he had had a similar attack that subsided spontaneously. At the time of admission he showed localized tenderness, without spasm, in the right lower quadrant. The white-cell count was 7600, with 65 per cent polymorphonuclears. The urine was normal. Although the findings were atypical, they were suggestive enough to warrant hospital observation. The next morning the patient had unmistakable measles. He was transferred to a hospital for contagious diseases, where abdominal signs promptly disappeared and did not recur.

CASE 3. P. W., a 9-year-old girl, was admitted to the Surgical Service on November 12, 1933, because of recurrent attacks of pain in the right lower quadrant and vomiting, the attacks had come with increasing frequency during the last year, and had required one previous hospital admission and many outpatient observations. Most of the attacks were accompanied by headache, usually on the left side. The physical examination was always negative save for minimal tenderness in the right lower quadrant. The white-cell counts were consistently around 9000 and the temperature was 100°F. Barium x-ray examination of the large and small bowel, an intravenous pyelogram, a cholecystogram and films of the skull were normal. The patient's mother had for years had similar symptoms, for the ineffectual relief of which a normal gall bladder and appendix had been removed at separate operations. Although the patient had been admitted for appendectomy, it was thought that migraine was the correct diagnosis. Operation was postponed. Under medical care the child improved.

CASE 4. M. M., an 11-year-old girl with recognized diabetes, was admitted to the Children's Hospital on September 20, 1938, because of right-sided abdominal pain of 6 hours' duration. The day before she had been nauseated, she had vomited several times on the day of admission, and was constipated. The pain was severe, had increased steadily and was localized to the right lower quadrant. She had had a series of eye infections (hordeola) during the previous week. In spite of the regular dose of 16 units of protamine insulin and 16 units of regular insulin daily,

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## CLINICAL NOTE

### A CERVICAL-SPINE BRACE WHICH REDUCES THE USE OF PLASTER CASTS

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THE cervical-spine injuries seen on the Neurosurgical Service at the Boston City Hospital are all associated with injury to the spinal cord. This condition necessarily modifies the handling of the patients, for the presence of cord damage usually implies enough dislocation to cause pinching of the cord, which is apt to mean that there is extensive ligamentous damage. Such dislocation, whether or not it is still present at the time of admission to the hospital, is prone to recur after the patient is up and about unless there is adequate external support for the neck.

Whatever type of treatment is given the patient during the early, acute stage of his course, flexion must be prevented because flexion invites further dislocation. In addition, one must apply traction to the neck to reduce any remaining dislocation and to steady the neck against the voluntary movements of the patient. On the Neurosurgical Service, flexion is prevented and traction applied by means of a head halter or, occasionally, by wires passed through adjacent burr openings in the skull (skeletal traction). Either of these methods is commonly continued for a period of six weeks. If by that time the patient has recovered enough neurologic function to profit by sitting up or even trying to walk, some rigid form of neck support must be applied. That is the problem with which this paper is concerned. The apparatus here described is not advocated for the early treatment of cervical-spine injuries with cord damage, except under such unusual circumstances as were present in Case 2. Instead, it is meant to be used after any pre-existing dislocation has been reduced, and after a certain amount of stability has been acquired by the spine during six weeks of immobilization in traction, and, in particular, as soon as the patient is able to be out of bed.

The application of a rigid support to a patient whose spine injury is complicated by cord damage is made more difficult because of such damage. Frequently these patients can use neither arms nor legs to help themselves, and they must be lifted, turned and handled with the greatest

care so as to prevent further cord damage. The need for care in handling such patients has long made us skeptical of the methods necessary to apply a plaster cast. Even in the best of hands, to say nothing of the efforts of junior house officers, the patient is subjected to what seems an undue amount of moving and manipulation under circumstances in which a single unguarded movement may cause further cord damage and permanent harm.

But this is not the only objection that experience has raised against the use of plaster casts. Patients with cord damage often have areas of cutaneous anesthesia, and it is well known that these areas withstand pressure, as from a cast,



FIGURE 1 Case 1  
*X-ray photograph showing anterior dislocation of the fourth cervical vertebra*

very badly and are prone to develop pressure sores. Furthermore, the weight of a cast is not an inconsiderable item for a patient whose motor power is so weakened by cord injury that merely supporting the weight of the body requires the greatest effort. A final contraindication is found in the looseness of the cast after it has been worn long enough to permit atrophy or weight loss from any cause to develop.

To avoid the disadvantages of plaster casts, we have tried other means of supporting fractured necks. Among these has been the use of a leather cuirass strengthened with iron braces. But such an apparatus, if it was to fit well, also required the making of a mold as a preliminary step. While the cuirass has advantages over a cast in the matter of weight and convenience, still the making of it requires approximately as much handling of the patient.

Finally, we were led to try an adjustable

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cervical-spine brace. The patient on whom it was tried was a nineteen year-old boy (Case 1, J B., No. 952827) who had suffered a fracture of the fifth-cervical vertebra, with marked anterior dislocation, in a diving accident (Fig 1) There

until it appeared that moderately firm union had occurred. By this time the patient was clamoring for relief from the collar, which was badly soiled and unsightly. Some kind of support was still necessary, however, and it had to be of such



FIGURE 2 Case 1

*Cervical support stabilized by attaching back brace*

was a complete dislocation of the articular facet on one side. The right arm and leg were completely paralyzed and there was hypalgesia below the level of the fourth cervical vertebra on the left, giving a Brown-Sequard syndrome. There was urinary retention, and lumbar puncture showed a partial block.

Halter traction was used for a period of four days, but was ineffective in reducing the dislocation. Skeletal traction was then applied for a period of seven weeks during which the vertebrae were gradually realigned and the neurologic signs disappeared almost completely. Eight weeks after the accident, the cervical brace\* shown in the frontal view in Figure 2 was applied. This has adjustable supports in front and in back, and it was thought that with reasonable co-operation on the part of the patient it would give adequate immobilization. But the patient could not be impressed with the need for limiting his activity and, as one might judge from the small amount of purchase that the apparatus obtains on the thorax, flexion at the cervicodorsal junction was not sufficiently restricted, and the vertebrae began to slip again. After a short period of halter traction to improve the alignment the patient was put into a plaster cuirass. This was not removed

a type as to immobilize the cervicothoracic junction. For this reason, a light iron back brace was



FIGURE 3 Case 1

*End result of treatment.*

attached to the adjustable collar previously used as shown in the last two views in Figure 2.

This provided a high degree of immobilization

\*Made by the Zimmer Manufacturing Company Warsaw, Indiana.



combined with the greatest ease of attachment and removal. It also permitted the patient to wash and shave, and the apparatus did not become un-



FIGURE 4 Case 2

*X-ray photograph showing fracture of the bodies of the fifth and sixth cervical vertebrae*

sightly as had his cast. Although the support was completely adequate, it still permitted a large amount of activity and was much more comfortable than a cast. The end result of treatment is shown in Figure 3

placement at the time the x-ray photographs were taken, he was unable to extend either arm, and only the left lower extremity showed a slight amount of voluntary motion. He was placed in head traction, and in the next three weeks recovered a small amount of function in all the paralyzed muscles. However, the threat of hypostatic pneumonia was ever present in spite of frequent changes of position, so that it was decided to get him out of bed much earlier than would have been risked with a younger patient. The combined neck support and back brace (Fig 5) were applied each time before getting him up in a chair, and halter traction was used when he was in bed. In the eight weeks after he first left his bed he was up a considerable part of each day. Functional recovery progressed to the point where he was able to manage his wheel chair and could walk a little with help. Progress thereafter was more rapid and now, five months after his injury, he is normally active in every respect. There was no pulmonary complication, and the cervical spine remains in good alignment.

#### CONCLUSION

Two cases are reported that illustrate the use of an adjustable cervical-spine brace which can be fitted and applied with a minimum of handling of



FIGURE 5 Case 2

*A seventy-eight-year-old patient in a combination brace*

Case 2 (M F, No 978915) illustrates another use for this type of neck support. This patient was a seventy-eight-year-old man who fell down stairs and fractured the fifth and sixth cervical vertebrae (Fig 4). Although there was little dis-

placement at the time the x-ray photographs were taken, he was unable to extend either arm, and only the left lower extremity showed a slight amount of voluntary motion. It is inexpensive. Its use avoids the disadvantages of plaster casts in treating cervical injuries with cord damage.

## REPORT ON MEDICAL PROGRESS

## CANCER

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## EXPERIMENTAL STUDIES

*Anatomy*

A HIGHLY significant contribution to elucidation of the mode of spread of malignant disease is the recent work of Batson<sup>1</sup> on the so-called "vertebral veins." This author by means of injections has demonstrated the richly anastomosing network of thin walled veins, relatively poorly provided with valves, extending from the cranium to the pelvis, surrounding the bodies of the vertebrae and roughly paralleling the vertebral column. There are frequent communications with the caval venous system as well as with the nutrient vessels of the bones, the vessels accompanying nerves, the vasa vasorum and the intracerebral and intraspinal veins. Through this venous system metastases from malignant disease and sepsis may be disseminated through the body without the necessity of passing through the lungs and heart. Batson suggests that this mode of transmission is probably a common one, notably in cases of carcinoma of the prostate and breast, and that it satisfactorily accounts for the paradoxical wide dissemination of metastases without apparent foci in the lung fields. Certainly the distribution of the injected material in some of the illustrated preparations coincides remarkably with the distribution of skeletal metastases from prostatic carcinoma. Ordinarily this venous system is relatively stagnant, and may hold pooled reserves of a considerable amount of blood. The flow through it is apparently accelerated by coughing and straining, which cause temporarily increased pressure in the caval venous column.

*Hormones*

Interest in hormones in relation to the etiology of cancer has been focused particularly on the problem of breast tumors. Lacassagne<sup>2</sup> summarizes what is known in this field, as follows: cancer can occur only in a mammary gland which has undergone a certain degree of development, development of the mammary gland depends on the presence of estrogenic and pituitary hormones, it is open to question whether the hormones have

any other relation to mammary cancer than that of bringing about the essential preliminary breast development. These conclusions bear out the earlier findings of Nathanson and Andervont<sup>3</sup> that the inhibition of mammary-tumor development by the use of testosterone is due to the inhibition of mammary development. Cramer<sup>4</sup> emphasizes the importance of this problem by pointing out that in mammary cancer the carcinogenic agent, if it is an estrogen, is a substance normally present in the body, and that it is therefore necessary to assume that it is present in excessive amount, or that it is not appropriately balanced and neutralized by other hormones, or that the susceptible person's tissues are unduly sensitive to normal amounts of the hormone.

Cramer and Horning<sup>5</sup> have drawn attention to a brown degeneration of the adrenal medulla in mice of high mammary-cancer strains. This degeneration is not secondary to cancer development, since it occurs in all individuals in the strain and not merely in those which develop mammary cancer. As a result of this degeneration a hormone antagonistic to estrogenic hormones is diminished in amount, thus resulting in a relative increase in the effective amount of the estrogenic hormone. It is evident that Cramer and his associates attribute more direct etiologic significance to estrogens in mammary cancer than does Lacassagne. Cramer believes that patients with mammary cancer must at some time have presented a hormonal imbalance, and that it is reasonable to hope that some means of detecting such an imbalance will be devised or discovered. It is likely that even if the former were true, the imbalance would antedate the onset of cancer by many years.

*Genetics*

Reference was made in last year's review<sup>6</sup> to Bittrner's<sup>7</sup> work on the effect of foster nursing on the incidence of mammary cancer in mice of high cancer strains. Murray and Little<sup>8</sup> have carried out further work on this subject, and conclude: "Some extra-chromosomal influence which is ten times as powerful as any possible chromosomal factor is instrumental in determining whether or not mammary cancer appears in the first out-cross generations. The tendency to have

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mammary cancer is not Mendelian in nature" Further studies are necessary before the nature of the extrachromosomal influence can be identified

Bittner himself has repeated his foster-nursing experiments with mice of high lung-cancer incidence. In these animals, contrary to the experience with mammary carcinoma, the foster nursing did not affect the expected incidence of the tumor in the offspring. He concludes that probably one Mendelian factor was involved for the transmission of pulmonary carcinoma susceptibility in mice.

### *Immunity and Metabolism*

Muus, Craig and Salter<sup>9</sup> induced varying degrees of immunity to an implanted tumor by Andervont's method. In this way the same transplanted tumor could be made to grow rapidly as a malignant tumor, or slowly as a benign one. This experiment clearly demonstrates that the degree of malignancy of a tumor is to a certain extent a measure of the defensive reactions of the host tissues. Careful metabolic determinations were carried out in an effort to determine differences between the benign and malignant modes of growth of the same tumor. There were no essential differences between the two as regards lactic-acid and ammonia production. Oxygen consumption was greater in the malignant mode of growth.

## GENERAL CONSIDERATIONS

### *Education*

The state departments of health of Massachusetts and Connecticut have each distributed a book on cancer to the practitioners of the states, with the object of providing authoritative descriptions of the signs, symptoms and proper methods of treatment of cancer of the various sites. The Massachusetts book, *Cancer: A manual for practitioners*, provides readable and scholarly chapters, each written by an authority in his particular field. It has been suggested that it would be an improvement if brief identification data for these authors were included. The book is well printed and bound, and will undoubtedly be preserved and referred to by its owners. Inevitably the information it provides will result in an improvement in the usual methods of managing cancer.

The Connecticut book, *Cancer: A handbook for physicians*, is smaller and less pretentious than the Massachusetts book. The chapters are written by various committees, rather than by individuals, and the resultant compromises of opinion as to methods of treatment are evident in many of the chapters. The essays are presented with

numerous subheadings, with statements of the well-defined stages of the diseases, and outlines of appropriate treatment for each stage. The treatments recommended have the approval of the Cancer Committee of the Connecticut State Medical Society, which has tried to standardize methods in order to permit comparisons and to facilitate end-result studies.

## RADIATION

### *Physiology*

Ewing<sup>10</sup> has attempted to account for the effectiveness of the divided-dose technics of radiation therapy on the basis of adaptation of the tissues. Normal tissues acquire a resistance to the dose, and by the third week of treatment can regenerate under the same dosage that initially caused destruction. Malignant cells cannot adapt themselves in this way, and hence the destructive action continues. Goldfeder<sup>11</sup> studied the respiratory changes in normal and malignant tissues in vitro following radiation. He found that the respiratory processes of the mammalian tissues are much less vulnerable than are the proliferative processes. Hence the effectiveness of radiation therapy against cancer must lie in its influence on the latter rather than on the former. Brues, Marble and Jackson<sup>12</sup> have carried out studies on the effect of colchicine in rendering tissues sensitive to radiation. They conclude that the administration of colchicine does not enhance or accelerate the effects of radiation in causing tumor regression.

### *Injuries*

Radiation injuries to various normal structures develop as a result of intensive therapy for malignant disease. Warren and Spencer<sup>13</sup> report a series of cases showing pulmonary damage and fibrosis, and a careful study of the histological injuries. Watson and Scarborough<sup>14</sup> emphasize the dangers of osteonecrosis of the jaw in the treatment of intraoral cancer. In a series of 1819 cases of intraoral cancer they encountered 235 cases (13 per cent) of osteonecrosis. Intestinal injuries secondary to radiation of carcinoma of the cervix are reported by Corscaden, Kasabach and Lenz,<sup>15</sup> while Todd<sup>16</sup> reports 24 cases of rectal ulceration from the same cause.

### *Supervoltage*

Numerous reports describing experiences with therapeutic use of voltages in excess of 200 kilovolts continue to appear. Mudd, Emery and Levi<sup>17</sup> believe that supervoltage is more effective than high-voltage therapy in cases of carcinoma of the cervix and prostate. They could find no advan-

tages in treatment with supervoltages in cases of carcinoma of the breast, pharynx or larynx. Leucutis<sup>18</sup> reports a series of 312 cases treated with 500 kilovolts and thinks that the results were superior to those secured with 200 kilovolts. Schmitz, Schmitz and Sheehan<sup>19</sup> report their result in treatment of carcinoma of the cervix by this method. Evaluation of the possibilities and field of usefulness of supervoltages will obviously require more time and experience.

### Radioactive Isotopes

The possibility of preparing radioactive isotopic substances which are identifiable in minute quantities has given tremendous impetus to investigation of the role and mode of metabolism of various substances in the body. The use of radioactive zinc, arsenic, phosphorus and so forth has permitted studies of the metabolism of insulin, arsenical drugs and phospholipids (Jones, Chalkoff and Lawrence<sup>20</sup>). The application of radioactive isotopes to problems of the therapy of malignancy is still in an experimental stage but offers great promise. Thus, Lawrence, Scott and Tuttle<sup>21</sup> have experimented with radioactive phosphorus in the treatment of leukemia.

### Cryotherapy

In a paper entitled "General Cryotherapy," Gerster and his colleagues<sup>22</sup> report four months' experience at the Lenox Hill Hospital with the "artificial hibernation treatment" of Smith and Fay.<sup>23</sup> The patients treated up to the time of their report were intensively studied in every respect, and the reports describe various aspects of the studies. Gerster's conclusions are of great interest.

It was possible to reduce patients' temperatures from 10 to 18° F. below normal for from a few hours to three days (counting from time 90° F. was reached on the way down to the time 90° F. was reached on the way out: totaling 2856 hours below 90° in sixty-five inductions on 26 patients).

Inductions can be repeated at intervals, as many as five times or more, depending on the patient's general condition.

Risks from pneumonia and from nephritis seemed not so great as might be expected.

In malignancies striking relief from intractable pain with discontinuance of narcotics was noted in 11 of 17 patients.

Sooner or later pain returned, sometimes less severe, in others just as severe as before treatment.

As time went on progressive cachexia was noted.

Perhaps if intervals between treatments were made shorter a difference in recurrence of pain and progress of cachexia might be noted. This is to be given a trial; we have not had enough experience.

Our material available during the past few months has not afforded sufficient experience regarding the ef-

fect of local refrigeration to justify drawing conclusions.

Paltauf<sup>24</sup> reports the histological and pathological material obtained in this study. Of 5 autopsied cases, 3 showed acute inflammatory lesions in the pancreas, which varied in degree from focal areas of necrosis to hemorrhagic pancreatitis with extensive fat necrosis. In 2 cases of breast cancer marked necrosis of the tumor tissue was noted in all the metastases. Paltauf was unable to find any regression of the primary tumors or metastases, "nor were we able to demonstrate unusual cell alterations or any changes which could be interpreted as effects of cryotherapy on the neoplastic tissue." Of the 27 patients subjected to general cryotherapy, 13 had died at the time of the report, and 6 had died within eight days of completion of the treatment. It seems likely that these deaths were hastened by the treatment.

Bischoff and Long<sup>25</sup> induced hibernation in mice with sarcoma. They found it possible to reduce the body temperature of mice below 20°C. for seven hour periods on five successive days, or for a continuous twenty-four-hour period. Their measurement of temperature was restricted to skin temperature observations. Careful study demonstrated no effect on the size or histology of the tumors as a result of such treatment.

It is probable that general cryotherapy will be found to be effective as a palliative procedure in certain cases with intractable pain, but it is doubtful whether it offers much hope as an effective weapon against malignant disease. In this connection it is interesting to note that Klinker<sup>26</sup> has demonstrated that a malignant cell can remain viable after chilling to a temperature of -200°C.

## REGIONAL CANCER

### Cystic Mastitis

Warren<sup>27</sup> has made a painstaking study of the relation of chronic cystic mastitis to cancer. Follow-up studies on all patients in whom a pathological diagnosis of chronic cystic mastitis had been made disclosed an incidence of breast carcinoma considerably higher than that expected. Warren's conclusion is that the condition is definitely pre-cancerous. This tendency is not so marked as to justify bilateral simple mastectomy in all cases in which the diagnosis is made. These patients, however, must be very carefully observed at frequent intervals throughout the remainder of their lives. The pre-cancerous tendency is apparently greater in younger women than in older women.

### Agnogenic Myeloid Metaplasia

Jackson, Parker and Lemon<sup>28</sup> have recently described a condition which they designate as "agnogenic myeloid metaplasia" of the spleen. The importance of this condition is that it has frequently been confused with leukemia. Radiation of the spleen is useless and possibly dangerous.

### Acid Phosphatase

Gutman, Gutman and Robinson<sup>29</sup> emphasize the fact that in carcinoma of the prostate there is an elevation of the level of the acid phosphatase in the blood serum. They suggest that a determination of this substance may help to distinguish between bone metastases of carcinoma of the prostate and Paget's disease of the bone. In the former condition the acid phosphatase is usually greater than 3 units per 100 cc.

### Fibrosarcoma

McNamara, Smith and Boswell<sup>30</sup> report a series of 16 autopsied cases of retroperitoneal fibrosarcoma. Metastases were present in only 2 cases. The authors conclude, "It may be assumed that if it were possible to detect the tumor at an early stage and to subject it to radical surgical extirpation, recovery would result." Warren and Meyer<sup>31</sup> studied lymph-node metastases of sarcoma. They found such metastases in 7 per cent of their cases of sarcoma, chiefly in patients with fibrosarcoma. They conclude that regional dissection offers some hope of cure in patients who apparently present regional lymph-node involvement.

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CASE RECORDS OF THE  
MASSACHUSETTS GENERAL HOSPITALANTEMORTEM AND POSTMORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 26381

## PRESENTATION OF CASE

A full-term normally delivered white male infant, weighing 9 pounds, was placed in the nursery immediately after birth. The infant was normal to physical examination and the mother enjoyed an uneventful postpartum course. The child had cried lustily and had a good color. He took his feedings well and to all criteria seemed to be a normal, healthy, baby. However on the second postpartum day the child became cyanotic during its 10:00 a.m. feeding of lactose. The cyanosis involved the face, lips and extremities. A carbon dioxide and oxygen mixture was administered, and the episode passed away. During the attack, physical examination revealed an active baby somewhat darker red in color than one would expect forty-eight hours after delivery. The heart was normal, the lungs clear. The fontanelles were soft, and the neurological examination negative. The tongue was normal the nose was not obstructed. X-ray films of the chest on the third day showed clear lungs, the heart was slightly prominent in the region of the right aortic arch, but there was no gross enlargement. Barium passed through the esophagus normally. On the sixth day the temperature rose to 100°F., and the infant lost 3 ounces of weight in a twenty-four hour period. The respirations were normal but the child continued to have a dusky color. The chest was clear, the fontanelles normal, there was no cough or sniffles. The child seemed vigorous and took 3½ ounces of formula at each feeding plus water between meals, he seemed well hydrated, and gained 1 ounce in weight. On the seventh day the temperature was 101°F. at 6 a.m., but it fell to 98.8 at 10:00 a.m. On the ninth day the child cried constantly as though he were in pain. There was a definite hypertonia particularly of the upper extremities and jaw which almost suggested trismus. The fontanelles were negative. The throat was poorly seen. The heart and lungs were negative. The abdomen was negative except for the presence of a small amount of gas. The umbilicus was healing well. Reflexes were active. A lumbar puncture was done. The fluid was not under increased pressure. About 20 drops

of xanthochromic fluid was removed over a period of ten minutes. A culture showed a moderate growth of colon bacilli.

At midnight of the tenth day after birth the baby began having a series of increasingly severe convulsions, each lasting two minutes or more. The temperature was 100°F., but it fell to 98 following the convulsions. The arms and legs stiffened cyanosis appeared and respirations ceased in deep inspiration. In ten to fifteen seconds these "spasms" of inspiration passed and breathing again occurred normally, although with an expiratory grunt. Luminal, calcium gluconate, and carbon dioxide and oxygen were administered but the convulsions recurred and became more severe. The respirations between the convulsive states became shallow and irregular. The heart rate remained around 160. In spite of all efforts the child quickly failed, and died on the tenth hospital day.

## DIFFERENTIAL DIAGNOSIS

DR. SIDNEY FARBER • I have been on the other side of the fence so long that this is a welcome change. If you hear any clinical remarks of strange import please remember that I am a pathologist.

It is stated that at birth the infant was normal to physical examination. In many cases an apparently normal physical examination may not be borne out by the future course of the infant. Signs of cerebral hemorrhage may develop, or anomalies in structure may manifest themselves within the next ten days or two weeks.

The child was cyanotic, and we are faced with the possibility of obstruction of the trachea rather than of the esophagus. We may be more apprehensive and think there might have been a tracheo-esophageal fistula or suspect that the feedings were a great effort for the baby and brought out cyanosis on the basis of some severe change elsewhere in the lungs, brain or heart. We may think of obstruction outside the trachea such as a vascular ring around the trachea and the esophagus, or of transposition of the great vessels.

I should like to make a generalization about the young infant. Positive physical findings are very important, changing physical findings are of considerable importance but negative physical findings are of very little importance. The heart was normal but no cardiac examination at this age can be so complete as to exclude congenital defects. The lungs were clear. We must recall that early interstitial pneumonia in the new

Asks professor of pathology Harvard Medical School, p. biologist,  
Children Hospital Boston

born is usually unaccompanied by physical signs

Cerebral hemorrhage may be present, although we should expect more in the way of respiratory symptoms. The fontanelles need not be bulging.

The tongue was normal. I have seen cyanotic attacks at this age due to hyperplasia of the tongue or macroglossia, these are produced by the tongue falling back on the glottis and thus causing respiratory difficulty, particularly during feeding.

The x-ray films of the chest on the third day "showed clear lungs." If Dr. Schatzki will permit, I shall make the same statement about x-ray examination, that is, clear x-ray films of the lungs do not rule out pulmonary disease, particularly if the changes be in the nature of congestion, edema or pneumonia, which are common findings at this age.

"The heart was slightly prominent in the region of the right auricle." That prominence at the right auricle may suggest congenital heart disease. We shall discuss that later. The prominence may be caused, of course, by the position of the normal thymus gland. I shall not consider the thymus gland as a possible cause of the cyanosis. There was no gross enlargement of the heart, but that finding does not rule out a congenital anomaly. The fact that barium was administered suggests that tracheo-esophageal fistula was excluded in the minds of the doctors. Had there been suspicion of a tracheo-esophageal fistula no barium would have been given, because of the danger of barium pneumonia. The barium passed through the esophagus normally, so any suspicion of atresia of the esophagus or stenosis of the esophagus may be dropped. It is possible that the barium may have been given to outline the left side of the heart, with the hope that a vascular ring around the esophagus might be outlined better in this manner.

The child seemed vigorous at this stage, presumably the cause of the difficulty was not great enough to disturb it, unless some other factor was added to the existing defect. Such variations in the temperature as are noted are consistent with bronchopneumonia or infection anywhere in the body in the neonatal period.

"On the ninth day the child cried constantly as though he were in pain." That is a very important symptom. It may point to central-nervous-system disease, with hemorrhage or meningitis. The cause for such crying may be pulmonary disease, such as pneumonia, or there may be a disturbance within the abdominal cavity, such as volvulus on the basis of malrotation of the intestine. Such a volvulus might repeatedly disengage itself without surgical help. An embolus on

the basis of congenital heart disease, lodged in an abdominal viscus might be the cause of such pain, or it might be explained on the basis of kidney disease, such as pyelonephritis.

"There was definite hypertonia, particularly of the upper extremities and jaw, which almost suggested trismus." Here we have symptoms definitely pointing to the central nervous system, although the damage might be no greater than that caused by cerebral edema secondary to bronchopneumonia. Because of the mention of trismus, we do suspect infantile tetany, but there was no Chvostek's sign or other evidence to lead us to consider the diagnosis more seriously. I drop it anyhow because tetany is somewhat beyond the province of the pathologist.

"The umbilicus was healing well." We may be misled by a healing umbilicus. Externally it may be normal in appearance but still be the site of an important infectious process. Organisms may enter, pass up the umbilical vein and enter the circulation while superficial healing is going on. There is no evidence, however, that the liver was enlarged, due to abscesses, nor were there other signs of a widespread inflammatory process.

"A culture of the spinal fluid showed a moderate growth of colon bacilli." We have no evidence in the nature of a smear of the fluid or a cell count to confirm the positive culture from the spinal fluid. It is hard to disregard a laboratory report, but I should like confirmatory evidence of meningitis. At this age meningitis caused by the colon bacillus is common. Ten per cent of all babies who die under one month of age die of meningitis, and the causative organisms, in the order of their frequency, are colon bacillus, pneumococcus, streptococcus and staphylococcus.

DR. TRACY B. MALLORY. No cell counts of the spinal fluid were made, or at any rate recorded, and no smears were stained for bacteria. Some red cells were noted, however.

DR. FARBER. With that report I shall have to consider colon-bacillus meningitis, but I cannot make a positive diagnosis without a finding of bacilli in a direct smear of the spinal fluid.

"The arms and legs stiffened, cyanosis appeared, and respirations ceased in deep inspiration." Here we have a series of changes that could be brought about by cerebral hemorrhage, meningitis or bronchopneumonia, with no alteration in the brain except edema.

"In ten to fifteen seconds these 'spasms' of inspiration passed and breathing again recurred normally, although with an expiratory grunt." These findings again may be caused by central-nervous-system disease or bronchopneumonia.

Luminal was given to quiet the patient calcium gluconate in the hope of relieving tetany if it were present, and carbon dioxide and oxygen on general principles, I suppose.

The two main problems here are cyanosis and convulsions. Cyanosis is by far the more important of the two findings, since convulsions did not occur until the end. The cause of cyanosis in the first ten days of life in the absence of positive physical findings is more often demonstrated at the autopsy table than explained before death at least in my experience. We look to the central nervous system, the lungs and the heart for the usual causes of cyanosis in the neonatal period.

Cerebral hemorrhage may occur even in the presence of normal physical findings at birth if the torn vessel is a tributary of one of the sinuses, provided that the vein of Galen is not torn. It is commoner to find a tear of a small vessel than of one of the great veins of the skull. Such hemorrhage, to be extremely important must be located beneath the tentorium. Small hemorrhages occur rather readily, particularly in the subtentorial region of the brain, because of the peculiar architecture of the brain in this area in the newborn. Cerebral hemorrhage may occur on the basis of asphyxia. We have no evidence of that in this patient. Meningitis has been mentioned as a possibility. Meningitis in the neonatal period may be secondary to bronchopneumonia or more often, to *otitis media* on the basis of hematogenous spread of the infection. Colon bacilli contained in infected amniotic fluid may enter the middle ear during delivery. If that is the case, at autopsy a smear of the middle-ear exudate will show, in addition to organisms numbers of cornified epithelial cells from the amniotic sac.

If we look to the lungs there are three things that might cause cyanosis: bronchopneumonia, which presumably developed late rather than early, since at first there were no definite signs pointing to the lungs, aspiration of amniotic sac contents, with vernix membranes outlining the alveolar duct walls and bronchioles—this may not be important as a cause of cyanosis until the second or third day when the foreign material has been drawn far into the lungs to form an effective barrier to the passage of oxygen from the air spaces to the alveolar wall capillaries, and congestion and edema secondary to cardiac disease.

The third cause of cyanosis at this age period is congenital heart disease. With a prominent right auricle we should suspect some change in the pulmonary valve or an interventricular defect. Anomalies of the aorta or calcified masses in the tricuspid valve may be the cause of cyanosis. I

mention bizarre types of congenital anomalies rather than simple ones because congenital heart disease to be the cause of death in the neonatal period must be exceedingly severe. I might mention transposition of the great vessels. Anomalies of the great vessels include as possibilities a vascular ring surrounding the trachea and esophagus, due to persistence of the fourth aortic arch,—a reptilian aorta—or some anomaly of the subclavian or left pulmonary artery so that pressure against the trachea or esophagus results. These are only possibilities, there is no means of making a definite clinical diagnosis of the exact type of a cardiac anomaly.

We might mention other possibilities. We have no evidence that the blood sugar was low; however, massive adrenal hemorrhage or a great increase in the amount of islet tissue in the pancreas has been noted as an explanation of both cyanosis and convulsions in the newborn. I will not go farther afield, but will commit myself to three general diagnoses. The first is congenital heart disease. My reason for mentioning that first is that there is no evidence that any other system was involved from birth as the primary cause of the prevailing difficulty and congenital heart disease may remain masked until additional strain is put on the circulation. The second is pulmonary congestion and edema, with terminal bronchopneumonia, and the third hemorrhage into the central nervous system, very likely below the tentorium. I must add as a possibility, as remote as all the others I have mentioned, colon-bacillus meningitis.

A PHYSICIAN. Subdural hemorrhage in older people produces symptoms in about this length of time, due to the absorption of fluid. Is this also characteristic of children?

DR. FARBER. I should have discussed that. Subdural hemorrhage is a possibility, although it is not the commonest cause of cyanosis in this age period.

DR. SCHATZKI. It is difficult to interpret the findings in a ray picture of the chest of a newborn baby. They are not reliable, so far as the heart is concerned. There is no way of diagnosing congenital heart disease at this age, unless the changes are very marked. There are no marked abnormalities in this case in regard to the size and shape of the heart. Another factor that enters into interpretation of the heart of a baby is the moment of respiration in which the film was taken. If the baby is crying one sees a decrease in the size of the heart and an increase in the size of the upper mediastinum with marked changes in the configuration of the heart and of the middle shadow. In other words one needs



fluoroscopy in a questionable case. From the films I should say that there is no evidence that there was anything wrong with the heart.

The situation in the lungs is different. If the films are good, one can be fairly certain as to whether or not there is pulmonary disease. There is no evidence of lung disease on this film.

A PHYSICIAN: Could this patient have had tetany?

DR. FARBER: I suppose it is a possibility. I have not heard of it in an infant of this age.

#### CLINICAL DIAGNOSIS

##### Convulsions

##### DR. FARBER'S DIAGNOSES

Congenital heart disease  
Pulmonary congestion and edema, with terminal bronchopneumonia  
Central-nervous-system hemorrhage, probably below the tentorium  
Colon-bacillus meningitis?

##### ANATOMICAL DIAGNOSES

Colon-bacillus meningitis  
Colon-bacillus septicemia  
Acute pyelonephritis  
Pulmonary congestion and edema

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: I think this case brings out clearly the difficulties with which the pediatrician is faced. The average stay of an adult in this hospital is seventeen days, and about half of that time is spent in making a diagnosis. Moreover the adult patient, unless acutely ill, can be put through the diagnostic mill with several types of examination during each day, which is quite impossible with a child. It is infinitely more difficult to accumulate the necessary data on a child, and almost invariably many of the things you would like to know are missing. However, one simple measure was needlessly omitted here which would have settled the diagnosis immediately. That was the examination of a gram-stained smear of the spinal fluid.

The clinical diagnosis on the death report that reached the laboratory was "convulsions." The autopsy showed that the primary disease was in the central nervous system. In the body elsewhere we found only two things. There was a severe grade of acute pyelonephritis, not foreshadowed by any of the symptomatology, and there was marked focal hemorrhage throughout the lungs. The latter, grossly, we thought was due to pneumonia, but on microscopic examination I can-

not be convinced that it is anything but hemorrhage and edema. The brain proved more interesting and showed marked meningitis, from which the colon bacillus was cultured. The heart's blood and the kidneys also showed colon bacilli in pure culture. The meningeal exudate in this case was in many places reddish-brown, a finding that suggests a considerable degree of hemorrhage. I am not familiar enough with colon-bacillus meningitis to know whether this is a characteristic finding.

#### CASE 26382

##### PRESENTATION OF CASE

A sixty-two-year-old clerk was admitted to the hospital complaining of low-back pain.

The patient stated that he had been ill in bed for one year at the age of sixteen. It was thought but never proved that the disease had been tuberculosis of the spine, as he had an attack of pleurisy at the onset of the illness, there were no other apparent signs of pulmonary tuberculosis. When he resumed activity he had a marked curvature of the spine, which persisted throughout his life. Until he was thirty he had suffered with "asthma." He otherwise enjoyed good health and led a moderately active life, being limited only by the dorsal kyphoscoliosis. With fatigue he had on occasions experienced low-back pain for many years. About three weeks before admission this became worse, especially at night. He consulted a dentist two weeks before entry, and two right lower molar teeth had been extracted, one coming out "whole" and the other "in several pieces." The next day the lower face and both eyes were swollen. Two days afterward, or eleven days before admission, these symptoms increased, and the low-back pain became acute. A physician found marked local tenderness over the left lower sacral region. A diagnosis of bursitis was made, and the pain was completely relieved by a local injection of no-vocain solution. However, the painless swelling of the right face and eyes continued to increase until about one week before entry, when it gradually began to subside. Three days before admission he developed slight "difficulty" in breathing, especially at night. He began to snore, and complained of an inability to breathe easily through the nose. There were no other symptoms. The remaining family, marital and past histories were non-contributory.

Physical examination revealed a somewhat poorly developed and poorly nourished man who had marked, fixed, right, mid-dorsal, structural scoliosis, with rotation on the convexity, and marked kyphosis. The face, especially the right side, was

edematous, particularly below the supraorbital ridges. There was slight cyanosis of the lips, fingernails and toenails. The superficial neck veins and the external jugular veins were engorged with the patient sitting upright, and the anterior chest and scapular regions of the back were covered with networks of engorged superficial varicosities. The skin in these areas was somewhat cyanotic. The pupils were small and equal and reacted well to light. However two days later another observer found them unequal, the right being two times larger than the left. Ocular motility and the visual fields were normal, but the retinal veins of the left eye were somewhat engorged. The veins of the right eye and both nerve heads were normal. The nose and ears were normal. The sockets from which the right lower molar teeth had been removed were healing fairly well. (X ray films showed a tooth fragment in the anterior socket this was removed and healing progressed uneventfully.) Otherwise the mouth, nasopharynx, oropharynx and larynx were normal. Because of the chest deformity examination of the heart was difficult. It was thought to be enlarged, and a blowing systolic murmur was heard. The blood pressure was 100 systolic, 80 diastolic. The pulse was regular and of good quality. The respiratory excursions were small. There were scattered crepitant rales in the right base and left mid-chest, laterally. The abdominal and rectal examinations were negative. Venous pressure was increased in both arms by rough test. The legs were normal. Throughout the examination the patient appeared drowsy and at times seemed to find it difficult to carry on a train of thought.

The temperature was 98°F., the pulse 90, and the respirations 22 per minute.

Examination of the blood showed a red-cell count of 4,400,000 with a hemoglobin of 12.0 gm (photoelectric-cell technic), a white-cell count of 6800 with 69 per cent polymorphonuclears, and an essentially normal blood smear. The urine was negative. Culture of the throat and the tooth sockets were negative for beta hemolytic streptococci. Blood cultures were negative. A blood-nonprotein nitrogen determination was normal.

Roentgenograms and fluoroscopy of the chest revealed a suggestive mass in the region of the right upper mediastinum. Intravenous injections of dye into the arm, to reveal venous channels, showed that no blood or dye returned by the subclavian vein, but rather by a collateral circulation.

He ran an irregularly downhill course. On the ninth hospital day, when a series of thirteen x-ray

treatments (200 to 300r daily) was begun, the patient developed an elevated temperature (99 to 102°F.), which persisted. For the first two weeks the facial edema and venous obstruction increased slowly, but a few days after roentgen therapy was stopped, it gradually decreased. Oxygen-tent therapy relieved the cyanosis and slight dyspnea. Chest plates taken three weeks after the completed treatments showed that the mediastinal mass was barely visible, there was an indefinite serrated margin, with no compression of the trachea. No cavities were seen, although a faint mottling had been noted on a plate taken the day when treatment was stopped. X ray films of the spine were inconclusive in regard to metastasis.

The patient developed urinary retention, with an atonic bladder, which required constant drainage. The urine became infected with large numbers of proteus bacilli, which on culture overgrew colonies of gram positive cocci in clusters. The white-cell count rose to 23,000 and he was given sulfanilamide. This caused malaise and cyanosis, and was discontinued. He gradually failed, and died on the fifteenth hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR EARLE M. CHAPMAN. I should like to call your attention to the facts that the chief complaint was low back pain and that according to the history he had had, when fatigued, low-back pain for many years, recently it had become worse, especially at night. This, of course, suggests bone pain.

Unfortunately there is no note of the type of anesthesia used when the teeth were extracted. We do not know whether it was done under local or general anesthesia. We do not know whether the pulmonary second sound was louder than the aortic, possibly because of the displacement of the heart, so controversy arises on that point. No lumbar puncture is recorded, although the patient had mental symptoms—drowsiness and so forth.

With so much deformity of the chest, it is very difficult to interpret the x ray film, but I presume this is the mass referred to. I can make out the heart fairly well and it seems to be enlarged. He has rather more prominence of the aorta than a person should have. This represents the curvature of the spine. The lung fields themselves are quite clear. Then by using a double exposure and a certain amount of rotation this area appears, which does not seem to be part of the spine and in which there are no normal structures. You can see the bronchus fairly well, coming down on the left side, and it appears to be normal. The trachea is normal. I do not see the bronchus of the right

lung, but it must be patent, otherwise the lung would not be inflated

His physician found tenderness over the lower sacral region. The lesion, if there is one, is not in the sacroiliac joint but in the ilium just above the acetabulum.

The record states that intravenous dye injections revealed that the venous channels showed no blood or dye returned by the subclavian vein but rather by a collateral circulation. Tumor and swelling were described on the right, so we can assume this was right. I take it the obstruction was mainly on the right.

DR. TRACY B. MALLORY: There is one point in the physical examination which seems to have been omitted in the record. On various subsequent physical examinations after the first one a unilateral wheeze was noted on the right—an expiratory wheeze.

DR. CHAPMAN: From the description it suggests obstruction of the right main bronchus.

DR. AUBREY O. HAMPTON: In this lateral film of the lower lumbar spine, there might be something here. It certainly is an abnormal appearance, but it is confused by the scoliosis and arthritic changes. With this process in the chest, which is also abnormal, you begin to wonder if the whole thing might not be metastatic cancer.

DR. CHAPMAN: If the body was tipped to the right side, do you think increased body weight could account for the changes in the spine?

DR. HAMPTON: Yes.

DR. CHAPMAN: I was asked to discuss this case because we\* studied cases of severe kyphoscoliosis two or three years ago in an attempt to explain the patients' sudden and often dramatic death. We investigated some ten or twelve cases at the Fatigue Laboratory at Harvard University. This case seems like a very bizarre and difficult situation to explain. It does not seem to fit into any of the patterns that we described. I should like to quote a word or two: "Those afflicted with severe chest deformities are greatly handicapped and rarely live to old age." This man lived to fifty-two. "Such deformities have occasionally proved fatal through secondary effects such as pulmonary infection, paraplegia or esophageal obstruction, but the most dramatic and probably the most frequent cause of death of the hunch-backed has been pulmonocardiac failure." Certainly this man did not have esophageal obstruction, and from the record as you hear it, it sounds as though pulmonary infection was suspected, because of the x-ray findings, and even tumor was

suspected, because x-ray therapy was given. However, these two diagnoses seem unlikely to me in view of the subsequent events. This man apparently did not have paraplegia, but there is some suggestion that he had pressure on the nerve roots or perhaps within the vertebral canal itself. The fact that he entered with an atonic bladder suggests cord pressure. He had back pain, but he had had it for many years, it grew increasingly worse and was finally his chief complaint.

There are two possibilities to explain this rather complicated picture. Obviously for the answer to either we need more information than is available from the case history. The first is that, because of the history of tuberculosis of the spine which we can accept, later in life one of the vertebrae crushed and he developed a paravertebral tuberculous abscess, which was described as the mass at the hilum or that Dr. Hampton described on the right. A mass at that level could produce a large pupil on the right. It could, by extension, eventually cause involvement of the subclavian vein on the right. It could even produce pressure on the right main bronchus, with the signs Dr. Mallory has suggested. It could also cause a thrombophlebitis inside the vein, and thus precipitate a final pulmonocardiac failure. He had tachycardia, rales in the chest, and a narrow pulse pressure. He was cyanotic and had an increased venous pressure, and finally died. So with these findings he did have pulmonocardiac failure. A paravertebral abscess along the spine causing pain and tenderness and finally a cord bladder is a possibility. The other is that he developed these symptoms of failure following tooth extraction. What kind of anesthesia did he have?

DR. MALLORY: Novocain.

DR. CHAPMAN: At least he had an operative procedure. We know that phlebitis in blood vessels does follow such a simple operation as tooth extraction. It is possible that following this he developed a thrombophlebitis in the innominate or subclavian vein, the field is right for such a complication because of this twist and torsion of the mediastinal contents, with probably some hindrance in the venous return. I should put this as a second choice.

Now what should we expect to find at autopsy? I believe that very likely he did have a break somewhere in the spine—one of the vertebrae crushed to produce a paravertebral abscess. There probably was a dilated and enlarged right ventricle, for this is the commonest finding at autopsy of kyphoscoliotic patients, this film shows enlargement at the base, but the heart appears to be of normal size lower down. Strangely enough in

\*Chapman E. M., Dill D. B. and Graybiel A.: The decrease in functional capacity of the lungs and heart resulting from deformities of the chest: pulmonocardiac failure. *Medicine* 18: 167-202, 1939.

kyphoscoliosis the majority twist to the right, very few to the left. That has led to one theory to explain pulmonocardiac failure, namely, that with the main curvature to the right, the compensatory curve to the left pushes the heart and squeezes it against the left chest wall. One thing that nearly all these patients have is a marked diminution in vital capacity. Unfortunately there is no record of vital capacity in this case. We know that in youth, when he was adjusting himself to an obviously diminished lung space this patient had a period of asthma.

As to the final handling of the case, which covers a period of several weeks, I can make no comment. He was given sulfanilamide and finally died. I believe the sulfanilamide played no role in the cause of death. I doubt if there were any toxic effects except that it did increase the cyanosis.

DR. JAMES S. STILLMAN: Sulfanilamide was given in small doses on the advice of the urologist. I do not believe he had a high blood sulfanilamide level, although a determination was not made. The cyanosis came on gradually a few days following the completion of x-ray treatment. Very slowly for a period of six weeks and very rapidly two days before death he began to develop the signs that had led to the fatal outcome. The reason a lumbar puncture was not done was that it was thought that the mental cloudiness was due to poor venous return and consequent anoxemia. The mental state cleared as soon as the anoxemia was relieved by an oxygen tent.

DR. CHAPMAN: Did he have engorgement of the veins to the left as well as the right?

DR. STILLMAN: Yes.

DR. ROBERT J. JOPLIN: The one thing that particularly interests me is the observation Dr. Hampton just made when he looked at the anteroposterior and lateral roentgenograms of the pelvis. These plates were taken in the Emergency Ward on the day the patient was admitted. At that time the patient had so much pain localized over the sacrum that he was unable to lie in bed on his back. After a very uncomfortable night he was brought into the hospital with the diagnosis of acute bursitis over the bony prominence of the sacrum and with the plan of injecting the bursa with novocain and washing it out with saline. Because this was an unusual place for a bursitis, it seemed fair to the patient to have an x-ray picture taken first in order to rule out any underlying pathologic condition that might be present.

and the wet plates were interpreted by the radiologist then on duty in the Emergency Ward as negative for any pathologic condition in the bone in that area. Therefore it was believed that the discomfort was due to a superficial condition. For this reason he was taken to the operating room. Novocain was injected with immediate relief of the pain. The area was irrigated in the usual way with normal saline. The patient had no more discomfort in the area following this procedure.

DR. RALPH ADAMS: I saw the patient in consultation after he had developed a classic mediastinal-pressure syndrome and had a unilateral wheeze. Since unilateral wheeze is practically diagnostic of bronchial obstruction, its appearance here was presumptive evidence of primary lung cancer. The amount of mediastinal compression was an unusual and confusing feature of the case.

I wish that someone would say a word about the response to x-ray therapy, because it is a matter of practical clinical importance.

DR. CHARLES S. KUBIK: Can you guess the type of cell that would show a good response?

DR. HAMPTON: The only cases reported here that have responded were those of the oat-cell type, and we naturally suspected such a tumor. It is difficult, I think, from the history to be certain whether the patient did respond. If it is true that he did respond to the treatment I should think that you would interpret the treatment as being evidence of carcinoma of the bronchus of a rapidly growing type.

#### CLINICAL DIAGNOSES

Lymphoma?  
Kyphoscoliosis.

#### DR. CHAPMAN'S DIAGNOSES

Tuberculosis of the spine  
Kyphoscoliosis  
Paravertebral abscess, tuberculous  
Cord bladder  
Terminal pulmonocardiac failure.

#### ANATOMICAL DIAGNOSES

Bronchiogenic carcinoma, with metastases to peribronchial and mediastinal lymph nodes, liver, spleen, adrenal glands and sacrum and extension to trachea and superior vena cava.  
Pulmonary emphysema, right middle lobe.  
Pulmonary atelectasis, left.  
Cor pulmonale, slight.  
Kyphoscoliosis, marked.  
Hydrothorax, bilateral.

Adenocarcinoma of prostate  
Prostatic abscess

#### PATHOLOGICAL DISCUSSION

DR MALLORY The postmortem showed, of course, an extreme grade of scoliosis, with marked changes secondary to that. It also showed thoracic cancer, the major part of the tumor being in the mediastinum, but there was also a tumor in the right upper lobe of the lung, which we thought was in all probability primary in the right upper-lobe bronchus. On microscopic examination it was a very highly malignant, rather small-celled carcinoma, with, however, numerous scattered giant cells. I hesitate a little to call it an oat-cell carcinoma.

We had a further surprise when we sectioned the prostate and found that that also was carcinomatous. This was a well-differentiated adenocarcinoma, and I cannot conceive of its having given

rise to such an undifferentiated metastasis as the tumor in the lung. I think it is more reasonable to assume that he had two independent carcinomas. There was also an abscess in the prostate, which was undoubtedly more responsible for the urinary symptoms than the carcinoma.

The fluctuant mass over the sacrum proved on incision to be a very large cavity through which ran all the fibers of the cauda equina, the posterior wall of the sacrum having been entirely destroyed by tumor. The tumor here was of the same type as the pulmonary tumor, not like the prostatic one.

The lungs also showed a well-marked emphysema of the right middle lobe, with a moderate degree of collapse of the left side, findings that you would expect in a scoliotic patient of this type. The heart was small and weighed only 225 gm. The right side was definitely hypertrophied, the ventricle measuring 6 mm in thickness, which one could call evidence of a slight *cor pulmonale*.

# The New England Journal of Medicine

Formerly the  
Boston Medical and Surgical Journal  
Established in 1828

OWNED BY THE MASSACHUSETTS MEDICAL SOCIETY AND  
PUBLISHED UNDER THE JURISDICTION OF THE COMMITTEE  
ON PUBLICATIONS

Official Organ of

THE MASSACHUSETTS MEDICAL SOCIETY  
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**MATERIAL** for early publication should be received not later than noon on Saturday.

**THE JOURNAL** does not hold itself responsible for statements made by any contributor.

**COMMUNICATIONS** should be addressed to the *New England Journal of Medicine*, 8 Fenway Boston, Massachusetts.

## AS I REMEMBER HIM

CERTAINLY no friend of Hans Zinsser, knowing his low opinion of orthodox obituary documents, could bring himself to write one about him. A sentimentalist at heart, he could not bear the thought of sentimental words used by others in relation to himself or his activities.

In deference then to his known wishes we choose to refrain from personal comment and let this scientist-poet speak for himself. In his latest published book,\* avowedly produced as a biography of "R. S.," he tells so well about himself what we all want to know that with the permission of his family and publishers we are printing excerpts from the last chapter.

But in those few minutes R. S. told me, something took place in his mind that he regarded as a sort of compensatory adjustment to the thought that he would soon be dead. In the prospect of death life seemed to be given new meaning and fresh poignancy. It seemed, he said, from that moment, as though all that his heart felt and his senses perceived were taking on a "deep autumnal tone" and an increased vividness. From now on instead of being saddened, he found—to his own delighted astonishment—that his sensitiveness to the simplest experiences, even for things that in other years he might hardly have noticed, was infinitely enhanced. When he awoke in the mornings, the early sun striking across the bed the light on the branches of the trees outside his window the noise of his sparrows and all the sounds of the awakening street aroused in him all kinds of gentle and pleasing memories of days long past which had left their imprint—indelible but, until now not consciously realized—of contentment and happiness. It was quite the opposite of the "woe of the remembering of happy times" in Canto V of the *Inferno* beginning "*Nessun maggior dolore*" and so on. R. S. felt a deeper tenderness for the people whom he loved, and a warmer sympathy and understanding for many whose friendship he had lost in one way or another. Each moment of the day every prospect on meadow or hill or sea, every change of light from dawn to dusk excited him emotionally with an unexpected clarity of perception and a new suggestiveness of association. Thinking of the shortness of the time still left him, he read—as though for a sort of P. P. C. conversation—the books that had meant much to him at the various stages of his life, and found them more moving more deeply wise, or more hilariously robust, according to their natures. Everything that went on about him or within him struck upon his heart and mind with a new and powerful resonance. So on the whole, he was far from either moping or dour sympathy.

As his malady progressed, he had another variety of experience which to some others more conditioned to religious belief than he was, might have signified an intimation of the separateness of body and soul.

He said to me "Here I am, me as always. My mind more alive and vivid than ever before my sensitiveness keener my affections stronger. I seem for the first time to see the world in clear perspective. I love people more deeply and more comprehensively. I seem to be just beginning to learn my business and see my work in its proper relationship to science as a whole. I seem to myself to have entered into a period of stronger feelings and saner understanding. And yet here am I—essentially unchanged except for a sort of distillation into a more concentrated me—held in a damaged body which will extinguish me with it when it dies. If it were a horse I was riding that went lame or broke its neck or a ship on which I was

\*Zinsser H.: *As I Remember Him*. The Biography of R. S. 443 pp.

traveling that sprang a leak, I could transfer to an other one and leave the old vehicle behind. As it is, my mind and my spirit, my thoughts and my love, all that I really am, is inseparably tied up with the failing capacities of these outworn organs."

"Yet," he continued, apostrophizing in a serio-comic mood, "poor viscera, I can hardly blame you! You have done your best, and have served me better than could be expected of organs so abused."

Though he had these spells of half-humorous revolt against the idea that his personality and his increasing joy of living should be so helplessly at the mercy of his deteriorating body, he was still grateful that, in his case, it was this and not the mind that was going to pieces first. He was not, at any time, tempted to seek strength in wishful surrender to a religious faith in which far greater men than he had taken refuge just before death. When this had, astonishingly, happened in the cases of several of his intimate friends, he regarded it as a capitulation of the mind to the fatigue of suffering. Indeed, he became more firm in his determination to see things out consistently along his own lines of resignation to agnostic uncertainty—as his father had done before him. Moving further away, therefore, from faith in any comprehensible conception of God, he yet grew closer in conviction of the wisdom and guiding integrity of the compassionate philosophy of Christ.

It is apparent, therefore, that in his last months, R S achieved a certain degree of philosophical tranquillity and resignation. It would be a mistake, however, to suppose that, apart from his purely personal reactions to his own fate and his immediate environment, he was less confused at the time of his death than I have described him in my introductory chapter. When he gazed beyond the circle of his own work, his family and friends, into the rushing world about him, he was completely bewildered. He had a little the same resentful feeling that he remembered having when, as a boy, he had walked through Normandy and had to jump into the ditch to let one of the recently invented automobiles rattle by—knowing that its passengers would have dinner at the town where he expected to arrive two days later. It was all moving too fast for him. Indeed, he was not sure whether the world that was rushing by was going forward or backward. He wondered whether he had not, perhaps, been born a little too soon and remained unable to catch up with his time. The world to which he had been born had not alone speeded up with that acceleration of which Henry Adams complained, but it had actually seemed to change direction. Scientific progress had brought as much sorrow as happiness. With immensely enhanced powers of production, millions were out of work and starving. Ideas of democracy and

individual freedom which he had accepted as the gradually evolved goals of centuries of struggle were not only being denied, but entire nations were frantically intent on destroying them. Great racial masses seemed willing to fight and perish, if necessary, for their own enslavement. New so-called "ideologies" were tearing up the foundations of all that men had thought firm and permanently established. Something had cracked in the old Western civilization, and its walls and lofty towers—cemented with the sweat and blood of their forefathers—were tumbling about men's ears. And the intellectual calamity seemed to be that no one could say whether the turmoil was the result of avoidable stupidity or of the operation of laws of economic and social evolution that were acting on mankind as other laws had acted on the dinosaur and the sabre-toothed tiger.

But in all these things he could never tell, before he died, whether the fault was in him or in the trends he disliked. He didn't admit this, of course, and remained, to the last, argumentatively arrogant. But I knew at the time of his death he was as thoroughly bewildered as any thoughtful individual of our time is bound to be.

As his disease caught up with him, R S felt increasingly grateful for the fact that death was coming to him with due warning, and gradually. So many times in his active life he had been near sudden death by accident, violence, or acute disease, and always he had thought that rapid and unexpected extinction would be most merciful. But now he was thankful that he had time to compose his spirit, and to spend a last year in affectionate and actually merry association with those dear to him. He set down this feeling in his last sonnet—

Now is death merciful. He calls me hence  
Gently, with friendly soothing of my fears  
Of ugly age and feeble impotence  
And cruel disintegration of slow years  
Nor does he leap upon me unaware  
Like some wild beast that hungers for its prey,  
But gives me kindly warning to prepare  
Before I go, to kiss your tears away

How sweet the summer! And the autumn shone  
Late warmth within our hearts as in the sky,  
Ripening rich harvests that our love had sown.  
How good that 'ere the winter comes, I die!  
Then, ageless, in your heart I'll come to rest  
Serene and proud, as when you loved me best.<sup>1</sup>

<sup>1</sup>Reprinted by permission of the *Atlantic Monthly*

## OLD WINE IN NEW SKINS

OCCASIONALLY the practicability, the economy and the health aspects of the paper milk bottle attract renewed attention, as at the present writing when the Milk Control Board is seeking to establish a fair price for milk so packaged. Various styles of paper bottles have been used for some years as containers in which milk can be vended, but nowhere, at least in and around Boston, have they become so popular as to constitute a familiar sight on the neighbors' back stoops.

The convenience of the non returnable milk bottle should be apparent from the consumer's point of view, although some education might be required before the housewife would accept a quart of milk with an invisible cream line. The producer's convenience should also be served, and if expensive bottle washing, sterilizing and perhaps capping machinery could be written off his books, a real economy in milk distribution would be effected.

It is, however, the question of health that is of the most concern and in this respect the differences between glass and paper containers are not so obvious as they might appear. The fundamental superiority of the paper container rests on the assumption that when it has once been used for milk it will not be so used again. In the majority of cases this undoubtedly obtains, but in other localities it is reported that the pitcher has gone not once to the well, but often. Fortunately paper will eventually disintegrate.

Since paper bottles cannot be steam sterilized, particular care should be taken that both the materials from which the product is made, including the water used in the pulp, and the various steps in its fabrication are under suitable control. This should include tests as to the number of bacteria per gram of disintegrated stock and per cubic centimeter of bottle rinse water. In this respect it is fair to say that paper bottles properly manufactured gave a much lower count on rinse water than do glass bottles washed under ordinary conditions.

Any consideration of paper milk bottles must inevitably bring to mind the great and increasing

use that is made of paper containers for various types of food that are susceptible to bacterial contamination—ice cream, salads, cottage cheese, oysters and other sea food. It is a matter of local pride that Boston has been a pioneer community in the recognition of the health potentialities of paper food containers, and has for some time had suitable legislation to deal with the problem.

## MEDICAL EPONYM

### DOVER'S POWDER

Promulgated by its inventor as a sovereign remedy for the gout this formula still persists, although in a greatly modified form, finding its chief present use as a means of "breaking up" a cold. Thomas Dover (1660-1741), M.B. and buccaneer published *The Ancient Physician's Legacy to His Country* (London: A. Bettesworth & C. Hitch, 1732), a book of medicine "designed for the use of all private families," which contains, among other things, what is probably the earliest description of rheumatic nodules. The following description of the powder appears on page 18:

Take Opium one Ounce, Salt Petre and Tartar vitriolated each four Ounces, Ipocacuanone one Ounce, Liguorish one Ounce. Put the Salt Petre and Tartar into a red hot Mortar stirring them with a Spoon till they have done flaming. Then powder them very fine after that slice in your Opium grind these to a Powder and then mix the other Powders with these. Dose from forty to sixty or seventy Grains in a Glass of White Wine Posset, going to Bed. Covering up warm and drinking a Quart or three Pints of the Posset Drink while sweating.

R W B

## MASSACHUSETTS MEDICAL SOCIETY

### SECTION OF OBSTETRICS AND GYNECOLOGY\*

RAYMOND S. TITUS, M.D., Secretary  
330 Dartmouth Street  
Boston

### PNEUMONIA AS A COMPLICATION OF THE PUERPERIUM

Mrs. I. R., a twenty-eight year-old para IV in labor was admitted to the hospital as an emergency on July 6, 1936.

A series of selected 10 Minutes by members of the section will be published weekly. Comments and questions by subscribers are not read and will be discussed by members of the section.



The family history was non-contributory. The patient's past history was not remarkable except for an operation for a "displaced womb and appendix" in 1932 and an attack of acute maxillary sinusitis and a tonsillectomy in 1934. She had been delivered by high forceps of a stillborn baby in 1929, and the next two deliveries were normal. Catamenia began at fourteen, were regular with a twenty-eight-day cycle and were not painful. The last period began on August 29, 1935, making the expected date of confinement June 5.

The pregnancy had been uneventful except for slight edema of the hands and feet a few days before admission. At that time the blood pressure and urine were normal. A general physical examination was negative except for edema of the ankles and hands. The fundus was three finger-breadths below the ensiform, with the vertex presenting and engaged. The fetal heart was heard in the right lower quadrant.

The patient had been in labor fourteen hours, and when she entered the hospital the cervix was fully dilated. The membranes ruptured shortly after entry. Before she had been fully prepared the head was bulging the perineum, and she was delivered spontaneously with median episiotomy, which was repaired a half hour after entry. Upon arrival at the hospital she had been given 3 gr of Nembutal by mouth, and she was given whiffs of ether during the delivery and repair. At that time she vomited a large quantity of undigested food and aspirated some of it, she was semiconscious at the time. After delivery of the placenta, the patient became cyanotic. The respirations increased, and the pulse rose from 104 to 160. The patient then began to cough, and expectorated some bright-red blood. The respirations were 40. She was given 1/3 gr of Pantopon and 1/150 gr of atropine and was placed in an oxygen tent. She was turned on her side with the head lowered to facilitate drainage. Within two hours the temperature rose to 104°F (rectal). During the night she regained consciousness but continued to have severe coughing attacks. The pulse remained 160 for eighteen hours, then gradually dropped. The temperature twenty hours after delivery was still 104°F (rectal). Two days after delivery it had dropped to 101°F and gradually to normal by the sixth day.

The patient was removed from the oxygen tent twenty-four hours after delivery. X-ray films of the chest at this time showed "extensive mottling

throughout the entire right lung and a similar, but less extensive, condition in the lower left chest." Physical examination showed moist rales throughout the entire right lung and at the left base, which disappeared about three days post partum. Repeat x-ray films on the ninth day revealed that the mottling previously noted had entirely cleared up. The patient was discharged on the tenth postpartum day.

*Comment* This case illustrates a serious complication that may follow inhalation anesthetics during labor, particularly when labor occurs soon after a full meal. The treatment was ideal and fortunately adequate.

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## STATED MEETING OF THE COUNCIL

A STATED meeting of the Council will be held in John Ware Hall, Boston Medical Library, 8 Fenway, Boston, on Wednesday, October 2, 1940, at 10 30 a m.

### *Business*

- 1 Call to order at 10.30 a m
- 2 Presentation of record of last meeting (Published in *New England Journal of Medicine*, 222 1040-1048, 1940)
- 3 Reports of standing and special committees
- 4 Appointment of an auditing committee.
- 5 Fill any vacancies in the offices of the Society
- 6 Incidental business

ALEXANDER S BEGG, *Secretary*

Councilors are asked to sign one of the two attendance books before the meeting. The Cotting Luncheon will be served immediately after the meeting.

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## CORRESPONDENCE

### RESULTS OF NOVEMBER, 1939, BOARD EXAMINATIONS

*To the Editor* I am enclosing a statement of the results of the November, 1939, examination conducted by the Board of Registration in Medicine.

STEPHEN RUSHMORE, M D, *Secretary*

State House, Boston

School	FIRST TIME		SECOND OR THIRD TIMES		FOURTH OR MORE TIMES		TOTAL		TOTAL APPLICANTS
	PASSED	FAILED	PASSED	FAILED	PASSED	FAILED	PASSED	FAILED	
Boston University School of Medicine	4						4		4
College of Physicians and Surgeons (Boston)	3	6	1	6	1	3	5	15	20
Harvard Medical School*	9						9		9
Massachusetts College of Osteopathy†		4	1	7		2	1	13	14
Middlesex University School of Medicine	8	11	14	29	2	14	24	54	78
Tufts College Medical School	8			1			8	1	9
Baylor University College of Medicine*		1						1	1
Chicago College of Osteopathy†		1						1	1
College of Medical Evangelists		1						1	1
Cornell University Medical College*	1						1		1
Creighton University School of Medicine*	1						1		1
Owensboro University School of Medicine	1	1					1	1	
Jefferson Medical College of Philadelphia	1						1		1
Johns Hopkins University School of Medicine*	1						1		1
Kansas City University of Physicians and Surgeons	1	1	3	10		5	4	16	20
Kirkcaldie College of Osteopathy and Surgery†		1		5	1	1	1	7	8
Mid-West Medical College	1	5		3	1	4	2	10	11
Missouri College of Medicine and Science				1				1	1
New York University College of Medicine*	1						1		1
Northwestern University Medical School	1						1		1
Ohio State University College of Medicine	1						1		1
Philadelphia College of Osteopathy†			3	3			2	3	5
Rush Medical College of the University of Chicago	1						3		3
St. Louis College of Physicians and Surgeons				1				1	1
State University of Iowa College of Medicine	1						1		1
Temple University School of Medicine*	1						1		1
Tulane University of Louisiana School of Medicine	1						1		1
University of Chicago School of Medicine*	1						1		1
University of Illinois College of Medicine*	1						1		1
University of Nebraska College of Medicine*	1						1		1
University of Pennsylvania School of Medicine*	1						1		1
University of Tennessee College of Medicine*	1						1		1
University of Wisconsin Medical School	2						2		2
Wayne University College of Medicine	1						1		1
Woman's Medical College of Pennsylvania	1						1		1
Anderson University Scotland*	1						1		1
McGill University*	1						1		1
Royal University of Norway*	1	1					1	1	2
University of Berlin	3						3		4
University of Bern	1				1		2		2
University of Bologna		1						1	1
University of Brera*	1						1		1
University of Brussels*	2						2		2
University of Edinburgh					1			1	1
University of Frankfurt*	1						1		1
University of Freiburg*			1					1	1
University of Geneva	1						2		2
University of Göttingen	1						1		1
University of Hamburg*	1	1					1	1	2
University of Königsberg*		1						1	1
University of Lausanne*	1		2				2		2
University of Milan	1						1		1
University of Munich		1						1	1
University of Naples		1				1		2	2
University of Paris	1	1		1				1	1
University of Prague*	1	1		1				2	4
University of Rome*				1				1	1
University of Strasbourg*	1						1		1
University of Vienna	8	1	1				9	1	10
	83	39	29	67	6	31	118	137	255

Approved schools.  
†Osteopathic schools.

Approved schools	70	12 <sup>1</sup>	8	2	1	2	74	16 <sup>1</sup>	91
Non-approved schools	13	21	18	59	4	23	35	9	112
Osteopathic schools		6	3	15	1	3	4	24	28
	83	39	29	67	6	31	118	137	255

\*The exponents represent graduates of European schools.

# ARTICLES ACCEPTED BY THE COUNCIL ON PHARMACY AND CHEMISTRY, AMERICAN MEDICAL ASSOCIATION

*To the Editor* In addition to the articles enumerated in our recent letter the following have been accepted

## Endo Products, Inc.

Ampoules Camphor In Oil—Endo, 0.2 gm (3 gr), 1 cc.

Ampoules Camphor In Oil—Endo, 0.2 gm (3 gr), 2 cc.

## Fhnt, Eaton & Co

Tablets Sulfanilamide, 5 gr

## Lederle Laboratories, Inc.

Tuberculin Patch Test (Vollmer)

Solution Liver Extract Parenteral—Lederle, 10 cc. vial

## Eli Lilly & Co

Ampoule Solution Liver Extract—Lilly, 15 USP units per cc. 10 cc size

Ampoule Solution Liver Extract—Lilly, 2 USP units per cc. 35-cc size

## Wm S Merrell Company

Thiamine Hydrochloride—Merrell

Thiamine Hydrochloride Tablets—Merrell, 10 mg

Thiamine Hydrochloride Tablets—Merrell, 30 mg

Ampuls Solution Thiamine Hydrochloride—Merrell, 10 mg, 1 cc.

Ampuls Solution Thiamine Hydrochloride—Merrell, 60 mg, 1 cc.

Ampuls Solution Thiamine Hydrochloride—Merrell, 100 mg, 1 cc.

## E. R. Squibb & Sons

Follutein—Squibb

Vials Follutein—Squibb, 500 international units

Vials Follutein—Squibb, 1000 international units

Vials Follutein—Squibb, 5000 international units

## U S Standard Products Co

Pituitary Solution, USP

Ampuls Pituitary Solution, USP, 1 cc

Ampuls Pituitary Solution, USP, ½ cc.

Vials Pituitary Solution, USP, 10 cc.

Vials Pituitary Solution, USP, 30 cc

## John Wyeth & Brother, Inc.

Tablets Sulfanilamide, 5 gr

Tablets Sulfanilamide, 7½ gr

Tablets Sulfanilamide, 10 gr

The following products have been accepted for inclusion in the list of articles and brands accepted by the Council but not described in NNR (*New and Nonofficial Remedies*, 1940, p 560)

## Lakeside Laboratories

Ampules Quinine and Urea Hydrochloride—Lakeside, 5 per cent, 2 cc. (for intravenous use)

Ampules Quinine and Urea Hydrochloride—Lakeside, 1 per cent, 1 cc. (for subcutaneous use)

Ampules Quinine and Urea Hydrochloride—Lakeside, 1 per cent, 5 cc. (for subcutaneous use)

PAUL NICHOLAS LEECH, *Secretary*

535 North Dearborn Street,  
Chicago, Illinois

# NOTICES

## ANNOUNCEMENT

CHARLES H KELLEY, M.D., announces the removal of his office to 37 Beacon Street, Boston

## BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will resume rehearsals under Alexander Thiede, on Thursday evening, October 10. Those interested in becoming members should communicate with Dr Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430)

## CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS, UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	ORTHOPEDIC CONSULTANT
Haverhill	October 2	William T Green
Lowell	October 4	Albert H Brewster
Salem	October 7	Harold C Bean
Brockton	October 10	George W Van Gorder
Gardner	October 15	Mark H. Rogers
Northampton	October 16	Garry deN Hough, Jr
Worcester	October 18	John W O'Meara
Pittsfield	October 21	Francis A Slowick
Hyannis	October 22	Paul L. Norton
Fall River	October 28	Eugene A McCarthy

## FORTY FIRST ANNUAL MEETING OF THE AMERICAN ROENTGEN RAY SOCIETY

The forty first annual meeting of the American Roentgen Ray Society will be held at the Hotel Statler, Boston, October 1-4

A symposium will be held each morning as follows: October 1, diagnosis and treatment of carcinoma of the larynx, October 2, classification, treatment and prognosis of carcinoma of the thyroid, October 3, unusual forms of pulmonary disease, and October 4, unusual gastrointestinal lesions and unusual sources of gastrointestinal hemorrhage.

A special clinical lecture of general interest will be given immediately after lunch each day, followed by individual instruction courses in the afternoon. Well known specialists throughout the country will conduct these scientific sessions.

There will be a special ladies' program. The annual golf tournament will take place on Monday, September 30. Conferences and general meetings are open to physicians and medical students, a fee is charged for the instruction courses. For further information write to Dr Frederick W O'Brien, chairman of the publicity committee, 465 Beacon Street, Boston

## SOCIETY MEETINGS AND CONFERENCES

SEPTEMBER 27-28—New England Surgical Society, Poland Spring, Maine.  
OCTOBER 1-4—Forty First Annual Meeting of the American Roentgen Ray Society. Notice above.

OCTOBER 6-11—Annual meeting of the American Academy of Ophthalmology and Otolaryngology. Page 81. Issue of July 11.

OCTOBER 8-11—American Public Health Association. Page 655. Issue of April 11.

OCTOBER 9—New England Dermatological Society. Page 390. Issue of September 5.

OCTOBER 10—Pentucket Association of Physicians.

OCTOBER 11-12—Pan American Congress of Ophthalmology. Page 698. Issue of May 23.

OCTOBER 14-25—1940 Graduate Portnight of the New York Academy of Medicine. Page 305. Issue of August 22.

OCTOBER 21—American Board of Internal Medicine. Page 369 issue of February 29.  
 NOVEMBER 13-14—New England Postgraduate Assembly Cambridge Massachusetts.  
 JUNE 4 1941—American Board of Obstetrics and Gynecology Page 34, issue of June 20.  
 MARCH 5—American Board of Ophthalmology Page 201 issue of August 1.  
 APRIL 21-25—American College of Physicians. Page 1065 issue of May 20.  
 JUNE 2-6—American Medical Association Cleveland Ohio.

#### DISTRICT MEDICAL SOCIETIES

##### WFOOLK

NOVEMBER 7—Oculars' meeting Page 305 issue of August 22.

##### WORCESTER

OCTOBER 9—Rutland State Sanatorium Rutland.  
 MARCH 13—Grafton State Hospital, Grafton.  
 DECEMBER 11—St. Vincent Hospital, Worcester.  
 JANUARY 8, 1941—Worcester City Hospital, Worcester.  
 FEBRUARY 12—Worcester State Hospital Worcester.  
 MARCH 12—Memorial Hospital, Worcester.  
 APRIL 9—Hahnemann Hospital, Worcester.

Supper will be served at 6:30 p.m. followed by business meeting and scientific program.

#### BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

*Physical Diagnosis* By William Nance Anderson B.Sc., M.D., associate clinical professor of medicine, University of Southern California School of Medicine Los Angeles California. 8, cloth, 424 pp with 92 illustrations. Philadelphia Lea & Febiger 1940. \$4.75

*Pharmacology and Therapeutics* By Arthur R. Cushny M.A., M.D., LL.D., F.R.S. late professor of materia medica and pharmacology University of Edinburgh Twelfth edition. Thoroughly revised by C. W. Edmunds A.B., M.D., professor of materia medica and therapeutics, University of Michigan, Ann Arbor Michigan, and J. A. Gunn, M.A., M.D., D.Sc., F.R.C.P., professor of pharmacology and director of the Nuffield Institute for Medical Research, University of Oxford, Oxford, England. 8 cloth 852 pp with 66 illustrations. Philadelphia Lea & Febiger 1940 \$6.50

*The Chinese Way in Medicine* By Edward H. Hume, M.D. 8 cloth 189 pp., with 8 illustrations. Baltimore Johns Hopkins Press 1940 \$2.25

*The Virus Life enemy* By Kenneth M. Smith F.R.S. 12 cloth 176 pp., with 19 illustrations Cambridge, England, University Press New York Macmillan Company 1940. \$2.00

#### BOOK REVIEWS

*Demonstrations of Physical Signs in Clinical Surgery* By Hamilton Bailey F.R.C.S. (Eng.) Seventh edition 8 cloth, 310 pp., with 377 illustrations. Baltimore Williams & Wilkins Company 1940 \$6.50.

In thirteen years this work has had seven editions, and there have been several impressions of four of them. Last

guess, Italian and Dutch are now in preparation. The work is popular because it is practical. The author states in the preface, "The scope and object of the book remain as before—essentially a demonstration of physical signs." The text is terse and helpfully supplemented by nearly four hundred well-chosen illustrations. The body is considered regionally in twenty six chapters. The physician is taught to use his eyes, his hands and his head, and to make each physical examination an exercise in the practical application of anatomy and physiology.

This small volume is well bound the typography is excellent and the calendered paper enhances the distinctness of the cuts.

*Injuries of the Skull Brain and Spinal Cord Neuro-psychiatric surgical and medico-legal aspects* Edited by Samuel Brock, New York University 8 cloth 632 pp., with 63 illustrations and 4 tables. Baltimore Williams & Wilkins Company 1940 \$7.00.

This book consists of a series of twenty-two chapters by various authors on injuries to the central nervous system. Such subjects as osteomyelitis of the cranial bones, thrombophlebitis, concussion and contusion of the brain, intracerebral hemorrhage, extradural hematoma, brain abscess, posttraumatic convulsive and allied states, neuroses following head and brain injuries, malingering, x-ray diagnosis of skull fracture and brain injury, birth injuries of the spinal cord and the effects of electric shock on the central nervous system are considered in the various chapters.

Most of these chapters are well written although a number of them leave much to be desired in regard to the style of presentation and the reduplication of statements. The book would have been greatly improved had the editor rewritten all the contributions for one of the best chapters—general considerations in injuries of the skull brain and spinal cord—is by him. The final chapter is on the medicolegal aspects of injuries of the skull brain and spinal cord. This is diffusely written giving a great deal of information about matters other than those right fully considered by the limitations of the title. Much of the material is, therefore, redundant this criticism could be easily applied to the whole book. Had it been carefully edited one estimates that the pages could have been reduced by a third.

The few illustrations and the format are excellent, and in general the typography is good. The type of paper used makes the book extraordinarily heavy—it weighs over three pounds. Although this book is of distinct value to the subject of a type that is badly needed one regrets that it was not edited with more care.

*One Way of Living* By James Bridie. 8 cloth, 290 pp. London Constable and Company Limited 1939 \$1.70

This is the amusing autobiography of a Scotchman who has achieved eminence, not only as a medical man but also as a journalist and a playwright—all this, by remaining quite passive in the hands of fate. But the amiable "cloth" which envelops him is of course no such thing. Dr James Bridie has a sharp mind, a keen memory, a wide acquaintance with men and matters, a sense of humor and an apparently unflinching sympathy with human foibles. In this war-torn and troubled world too often one has difficulty in driving oneself to read this

*The Surgery of Pain* By René Leriche, M.D. (Lyon), LL.D. (Glas.), FRCS Eng. (hon. causa), and so forth. Translated and edited by Archibald Young. 8°, cloth, 512 pp., with 18 illustrations. Baltimore: Williams & Wilkins Company, 1939. \$6.50.

Halsted once pointed out that hemorrhage, sepsis and pain were the particular problems of the surgeon. Much has been accomplished toward the solution of the first two which can be measured and studied objectively, but pain, inherently subjective and personal, and often apparently unaccompanied by organic disease, has remained largely an enigma. The investigation of pain has not, perhaps, attracted so many keen minds as have other less vague fields. The appearance of a book therefore by a surgeon who has devoted the greater part of his energy and time for more than twenty five years to the study and alleviation of pain is a noteworthy event.

The volume, consisting of nineteen lectures delivered at the *College de France*, is admirably translated by the late Professor Young, of Glasgow, who also summarizes the author's clinical and investigative experience at Strassburg. There is much theorizing and fine Gallic reasoning, with a liberal sprinkling of philosophy, but the tone in general is practical. Many of the author's concepts will find little support in this country, but their originality cannot be denied. The style is unusual in a medical book, and refreshingly far from dry or pedantic. Angina pectoris, the various neuralgias, including trigeminal neuralgia, and the pain of terminal malignancy are particularly well discussed.

Of timely interest, in view of the current war, are the author's views regarding causalgia, painful cicatrices and amputation stumps. The book is highly recommended to all surgeons.

*The Diagnosis and Treatment of Diseases of the Esophagus* By Porter P. Vinson, B.S., M.A., M.D., D.Sc., F.A.C.P. 8°, cloth, 224 pp., with 98 illustrations. Illinois: Charles C. Thomas, 1940. \$4.00.

There has long been need for a comprehensive book on the esophagus by a competent authority. Vinson's lifelong experience in the handling of patients with esophageal disease makes him eminently qualified for the task. Written from the standpoint of a physician and endoscopist, it covers, in sixteen chapters, dysphagia, esophagocopy, carcinoma, cicatricial stricture, congenital stricture, cardiospasm, diffuse spasm, diverticula, hysterical and functional dysphagia, injury and perforation, benign tumors, varices, fungous infections, syphilis, tuberculosis, esophagitis, foreign bodies, fistula, extra-esophageal lesions and gastroscopy. The bibliography, totaling 441 references, is conveniently subdivided at the end of each chapter. No attempt is made to describe surgical technic, but indications for surgery are discussed.

Although in general it is possible to agree with the author's ideas in the management of esophageal disease there are two important subjects, carcinoma and cardiospasm, with which many would disagree.

In the diagnosis of carcinoma, Vinson advises three methods of examination in the following order: x-ray, passage of sounds over a previously swallowed silk thread, and esophagocopy. He suggests the passage of sounds in order to determine the density and length of the stricture and to get small fragments of tissue for microscopic study. While all would agree that x-ray examination is of first importance, most esophagologists would say that endoscopic examination should come next, not only for direct inspection and bouginage, but particularly for bi-

opsy. The passage of sounds over a thread is of value in treatment but rarely in diagnosis. Vinson does well to emphasize this method of treating carcinoma of the esophagus, for all too frequently an unnecessary gastrostomy is performed, perhaps allowing the esophagus to close down completely and often depriving the patient of the pleasure of eating. Furthermore, as he points out, gastrostomy in debilitated patients carries with it a mortality of 10 to 50 per cent. It seems to the reviewer that Vinson overestimates the discomfort and risk of esophagocopy, and certainly his figure of 25 per cent negative biopsies is much too high. Furthermore, no mention is made of the fact that esophagoscopy may disclose lesions not demonstrable by other methods of examination.

The other point which seems worthy of comment concerns the treatment of cardiospasm, here the author discusses bouginage over a thread, the use of the hydrostatic dilator and various other methods, but he makes no mention of the Hurst mercury bougie. When it is considered that this last method is particularly safe, simple and efficacious, it seems that it should be included in any discussion of the treatment of cardiospasm.

Although, as previously noted, it is possible to find statements with which many would not agree, the book as a whole is excellent, it is well illustrated, and presents a great deal of valuable and unusual information. Every esophagoscopist and most gastroenterologists should read this book, and many of them should purchase it for their libraries.

*Fluorine Intoxication* By Kaj Roholm, M.D. 4°, paper, 364 pp. London: H. K. Lewis & Company, Ltd., 1937. \$4.03.

This book is a thorough and well presented study covering various aspects of fluorine intoxication.

Acute fluorine intoxication may be caused by the inhalation of fumes of gaseous forms of fluorides (or hydrofluoric acid), or by the ingestion of dissolved or easily soluble fluoride compounds, most commonly encountered as insecticides or rat poisons.

Chronic fluorine intoxication is of recent recognition. Fluorine has been found to have a specific effect on osseous and dental tissue. Mottled teeth, a dental disease endemic to man in certain geographical areas, has been traced to the relatively high fluorine content of drinking water. In individuals working with cryolite, — a double fluoride of sodium and aluminum, — osteosclerosis has been noted as an occupational disease. In herbivora in the environs of certain factories in Europe chronic intoxication has resulted in a disease like osteomalacia. *Darmouth*, a dental and mandibular disease, in herbivora in certain parts of North Africa, and *Gaddur*, a dental and bone disease, in herbivora in Iceland after volcanic eruptions have also been traced to chronic fluorine intoxication.

As in the introduction, the review of the role of fluorine in biology provides a good background and foundation of the subject. The author's original investigations, his study of spontaneous cryolite poisoning and his experimental work on animals are clearly presented. Individual topics are thoroughly covered. The discussion and general conclusions summarize the major points. An extensive bibliography is appended, and the text has numerous charts and photographs.

Although the study is sufficiently extensive to be considered a reference book of primary interest to those dealing with fluorine problems, the non-specialist with interest in its related fields will find it well written and interesting.

# The New England Journal of Medicine

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VOLUME 223

SEPTEMBER 26, 1940

NUMBER 13

## THE TREATMENT OF PROSTATIC OBSTRUCTION\*

REED M. NESBITT

ANN ARBOR MICHIGAN

PROSTATIC obstruction is produced by three pathologic entities, — carcinoma contracture of the vesical neck, and benign hyperplasia, — and until non-surgical methods are developed for either the prevention or the cure of these lesions, their treatment must remain operative. It is the purpose of this discussion to consider some of the pertinent points concerned with the selection of operation.

The choice of operation for cancer of the prostate should depend on the size and extent of the neoplasm. Most surgeons agree that radical perineal prostatectomy offers the greatest hope for cure of localized carcinomas which have not metastasized. A few outstanding specialists in perineal prostatectomy have advocated this operation for lesions showing local extension, holding the view that removal of the primary neoplastic focus provides a longer and more comfortable period of life than do less radical procedures. Personal experience and individual technical skill are important factors in evaluating the limitations of operation in this situation.

Infiltrating carcinomas of moderate size appear to do better with transurethral resection of the obstruction than with other methods of removal. Although many of these patients live for surprisingly long periods of time without developing further obstruction many others require repeated transurethral resection. It is my belief that patients with extensive and massive carcinomas are afforded greatest comfort by suprapubic drainage.

The value of various forms of irradiation therapy in the treatment of prostatic cancer has not been clearly demonstrated. The rare circumstances in which marked regression of the tumor

occurs following interstitial or external irradiation undoubtedly warrant a continued employment of these agents.

External irradiation affords marked relief of pain resulting from spinal metastases in most cases, and should be employed in preference to other palliative measures.

All urologists agree that contracture of the vesical neck or median-bar obstruction is best treated by transurethral resection. Some have gone so far as to proclaim that transurethral resection finds its ideal application in this group of cases. While it is true that occasionally one encounters a median bar that constitutes such a localized lesion that a simple transurethral excision relieves obstruction and cures the patient too frequently the process of sclerosis has involved not only the posterior vesical lip but also the entire prostate gland and the surrounding structures and interferes seriously with the normal functioning of the whole vesical outlet as well as that of the prostate gland and seminal vesicles. My experience with this group of patients has demonstrated that many empty their bladders following operation but continue to have increased frequency and difficulty with voiding, with discomfort in the region of the bladder, prostate gland and seminal vesicles.

In my hands, the greatest incidence of imperfect functional results following transurethral resection occurs among this group of patients. Bearing this fact in mind one is led to wonder if perhaps some of the surgeons who have condemned the operation have based their judgment on an experience in resection confined to this particular type of case. Other operations of greater magnitude designed to relieve the symptoms of contracture of the vesical neck produce no more favorable results than does resection so that this procedure should remain the operation of choice for such conditions.

\*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1940.

From the Department of Surgery, University Hospital, Ann Arbor, Michigan.

Associate professor of surgery, University of Michigan Medical School, in charge of Section of Urology, University Hospital.

Benign hypertrophy is today treated by three methods of approach the suprapubic, the perineal and the transurethral. The evolutionary development of the two open methods of prostatectomy has been so long and gradual that the medical profession as well as the lay public have had an abundant opportunity to evaluate them. Modern transurethral resection has developed during the past decade. Its evolution during that period has been accompanied by many growing pains, and some of its critics have overlooked the fact that the evolution and perfection of suprapubic and perineal prostatectomy produced many poor results and a mortality that now seems shocking. Those urologists who have participated in the development of transurethral resection, and who now continue to select it as the method of choice where they consider it indicated, must believe that it compares favorably with other methods of prostatectomy. Their evaluation must of necessity be made from a different perspective than that of the profession at large or urologists who disapprove of the operation. The evaluation by the lay public will eventually depend on an appraisal by the patient himself, and his opinion will be based on three factors: the discomforts attendant on the immediate postoperative period, the duration of hospitalization and the functional end result. I believe that uniformly good results may be obtained if certain fundamental principles of management are adhered to.

A discussion of some of the most serious complications that have tended to discredit transurethral resection, and of certain refinements in the technic of operation which have been devised in order to avoid them, may be of some interest. These complications are, first, infection and sepsis during the immediate postoperative period, second, traumatic stricture of the pendulous portion of the urethra, and third, persisting urinary dysfunction, with cloudy, infected urine, delayed urinary sepsis and occasional recurrent hemorrhage.

Since infection plays an important part in the morbidity and mortality of operation, its control and prevention are imperative. To perform a complete transurethral prostatectomy and have the patient die of sepsis is a sad commentary on the surgeon and the operation he has performed. It is probably true that sepsis occurs more frequently as a result of the introduction of bacteria foreign to the patient than it does from organisms that the host brings with him to the operating table. The careful preparation of the patient for catheterization or instrumentation and the aseptic

care of catheters and drainage systems, before and after operation, will in a large measure reduce sepsis to the status of an unusual complication. It has been my practice to employ a closed, sterile irrigator drainage system (Fig 1) for all

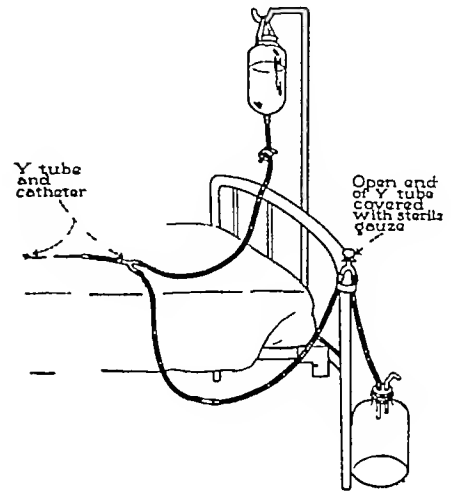


FIGURE 1 The Irrigator Drainage System

*One end of the Y tube between the catheter and drainage bottle is left open in order to prevent negative pressure on the bladder. This open end is covered with sterile gauze. The Y-tube level can be regulated to suit purposes of decompression.*

patients requiring catheter drainage before operation, and its use is part of the postoperative routine. The entire system, wrapped in a sheet, is sterilized in the autoclave. Each ward has an available supply. Catheters are introduced with aseptic technic, and the irrigator drainage system is immediately connected. In most cases the reservoir bottle is filled with 2 per cent boric acid solution. When the bladder is grossly infected, 0.25 or 0.50 per cent acetic acid is employed. Frequent irrigations with this solution quickly clear up most severe bladder infections. The irrigator system is never disconnected when once put into use, the object being to provide drainage and to prevent the contamination of the bladder by accidental inoculation with organisms foreign to the host. The absence of sepsis which has resulted from the employment of these methods has justified a great enthusiasm for them.

The ultimate result of a perfectly performed resection has occasionally been marred by the development of urethral stricture. This unfortunate sequel has been observed by all resectionists who have checked up on their patients, but unfortunately has received practically no recognition in the literature. Bumpus<sup>1</sup> aptly remarks that one had better perform some other type of prostatec-

tomy than do a successful resection and leave the patient with a lesion of the urethra infinitely more debilitating and difficult to treat than his prostatic tumor.

Resectoscopes must of necessity have sheaths of large caliber, most instruments in common use being No 28 or 29 Fr in size. Not all male urethras are of this caliber. It has been the practice of resectionists to dilate such urethras until they can accommodate the resectoscope. Some have even performed internal urethrotomy to attain the desired accommodation for large instruments. In either event the dilation has amounted to rupture or division of the urethral mucosa which can only result in stricture. Such an injury invariably occurs in the pendulous portion and at the penoscrotal angle, where strictures are apt to contract rapidly and are notoriously hard to dilate. The anticipated success of resection has doubtless led to occasional unwarranted disregard of the urethra and in some cases to irreparable result. Perineal urethrotomy (Fig 2) has been dem-

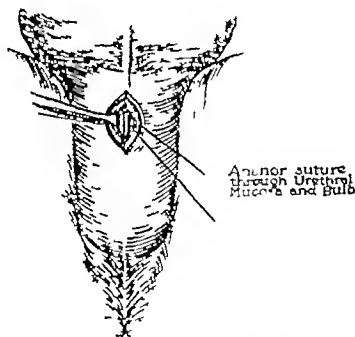


FIGURE 2. Perineal Urethrotomy

Anchor sutures of catgut are introduced through entire thickness of bulb and the urethral mucosa. These aid in introducing instruments into the urethra and facilitate closure of bulb after operation.

onstrated to be a method of averting this disaster, and I have employed it in all cases in which the urethra has not easily admitted the free passage of a No 30 Fr steel sound. Also in rare cases in which unusual maneuverability of the instrument was desired and the prostate was excessively long I have elected to make this approach, even though the urethra could have easily accommodated the standard resectoscope. When urethrotomy has been performed the catheter may be introduced either through the incision or through the entire urethra following operation depending on the

amount of pre-existing urethral disease. When the catheter is brought out through the meatus I usually take one suture in the bulb at the site of the urethrotomy incision. A small gauze pack is then introduced into the wound and left in for twenty-four hours. If the wound is not packed in this way the skin frequently closes by first intention and a small subcutaneous abscess is apt to develop. These wounds invariably close promptly and have not in my experience been followed by any unfavorable sequelae.

During the early days of resection there appeared authoritative statements to the effect that the enlarged gland would shrink in size if one but removed the tissue actually giving rise to obstruction, channelizing the prostatic urethra. Experience has shown that this advice was wrong in that a gland so resected not only fails to shrink but frequently acts as a focus for urinary sepsis. The researches of Flocks<sup>3</sup> have been of tremendous value, not only in providing an understanding of the pathologic anatomy of prostatism but also in explaining the reasons for many of the postoperative complications that have tended to discredit this operation. Flocks has shown that most of the hypertrophic mass of tissue derives its blood supply from the urethral arteries, which enter the prostate in the region of the internal sphincter and course distally in the substance of the lateral lobe. In transurethral resections these vessels are cut across and thrombosed at their point of entry into the gland. If the tissue supplied by them is not removed at operation it necessarily undergoes varying degrees of devitalization and may become infarcted throughout a considerable area. Patients harboring such septic infarcts may suffer recurrent obstruction persisting abnormalities of urinary function, urinary sepsis and delayed hemorrhages. Their primary need for prostatectomy has not been supplied and relief from the disability is dependent on the completion of the prostatectomy by either the transurethral route or some other. Thus the researches of Flocks, as well as clinical experience, have abundantly demonstrated that transurethral resection must be in fact transurethral prostatectomy. Surgeons who perform this operation must be sufficiently aware of their own technical limitations to employ it only when the gland is of such a size that a more or less complete removal of tissue can be expected.

Space does not permit a description of the technique of transurethral prostatectomy but one feature of it which I believe to be essential to adequate removal of tissue, will be discussed that is, three dimensional perception. The instruments that have been regularly used to perform this opera-



tion provide only visual perception of two dimensions. Perception of the third dimension can be obtained only through the sense of touch by rectal palpation, enabling one to estimate accurately the amount of tissue that must be excised. Pressure exerted upward or medially by the examining finger also aids materially in bringing tissue into the path of the cutting loop or blade of the instrument. Guided thus by the sense of touch, as well as by sight, one can avoid the dangers of cutting too deeply in vulnerable areas and can carry resection of tissue accurately down to the readily recognized capsule of the gland. Modifications of the resectoscope have been made available so that the operator can now work the instrument entirely with one hand, leaving the other hand free to guide safely the excision of tissue. The use of this modified instrument has permitted not only a refinement of technic from the standpoint of accuracy and safety, but also an increase in the speed of resection.

I am inclined to believe that excessively large glands are more advantageously removed by perineal prostatectomy than by multiple-stage resection. A comparison as to the mortality, comfort to the patient and length of hospitalization may well show the advantage of perineal prostatectomy in this type of case. At the present time I confine my indications for resection to benign hypertrophies of a size that will permit the completion of a subtotal prostatectomy in one operation of an hour or less. The fact that secondary resections must be performed in 6 per cent of the cases indicates that my judgment of size is not infallible. However, the secondary resections necessitated by these occasional errors in judgment are always minor affairs that take but a few minutes and do not appear to increase morbidity or materially lengthen the period of hospitalization. It is the repetition of prolonged and extensive resections that I strive to avoid wherever possible. I am performing perineal prostatectomies for glands of larger size, and expect to conduct a critical evaluation of the two procedures at a later date when a considerable series of cases has accumulated.

Very few reports have appeared which give the end results following transurethral prostatectomy. The difficulties of obtaining complete follow-up are well known, but such reports are available for an appraisal of the open methods of prostatectomy and more should be available for the transurethral procedure. A recent follow-up has been conducted to compare the end results following transurethral resection performed at the University Hospital with those following perineal prosta-

tectomy performed by an outstanding urologist elsewhere. One hundred consecutive patients were sent questionnaires from each clinic. All these cases had been operated on from six to eighteen months previously, and all were cases of benign prostatic hypertrophy. A detailed account of this joint investigation will be reported in the near future. The comparative results cannot appropriately be presented at this time, but it can be stated that except for the factor of urinary control the results of the two procedures in these series are practically identical.

For the purpose of evaluation of the transurethral operation, certain of the data regarding our series are presented in Table 1.

In tabulating the results of operation it is of some interest to compare the statistics compiled from the recent study with a follow-up<sup>3</sup> carried

TABLE 1 *Data on Patients Who Underwent Transurethral Resection*

Age	
Average	68 yr
Youngest	48 yr
Oldest	85 yr
Complete retention prior to admission	55%
Preliminary preparation (over 24 hours) in hospital before operation	25%
Patients operated on without preparation by catheter drainage in hospital	75%
External urethrotomy performed on account of small urethra, severe urethritis or high situated prostate	25%
Amount of tissue removed at operation	
Average	39 gm
Smallest	12 gm
Largest	170 gm.
Number of resections employed	
Single	94%
Two	6%
More than two	0
Postoperative days in hospital	
Average	13 days
Shortest period	5 days
Longest period	27 days

out in 1934, when a comparison was made between transurethral and suprapubic postoperative cases operated on in the University Hospital. In that study a group of 313 cases of benign hypertrophy treated by resection were compared with 100 suprapubic cases. These three groups are compared in Table 2. In this tabulation the suprapubic operation suffers by comparison with both transurethral series. The comparison is probably an unjust one because the suprapubic cases were operated on coincidentally with the resection cases represented in the 1934 report, and were not so favorable in so far as complications of obstruction were concerned. These patients were nearly all put on suprapubic drainage because of renal insufficiency, severe infection, calculi or excessive size of the prostate.

The recent transurethral series shows to considerable advantage over the previous series in all points of comparison. It is my belief that various refinements in technique have contributed materially to these improved results, and it is my hope that further refinements in the technique of opera-

TABLE 2. Comparison of End Results

QUESTIONS	TR. RESECT. (1934)	OPEN (1934)	TRANS. (1940)
	%	%	%
Do you old with perfect comfort?			
Yes	9	90	99
No	3	10	1
Do you have perfect control?			
Yes			100
No			0
How many times do you old each day?			
2-3	16	1	35
4	29	2	39
5	1	30	9
6	13	16	12
7	25	30	5
How many times do you old each night?			
0	16	6	45
1	2	47	31
2	22	70	14
3	19	16	5
4	8	2	4
Over 4	8	16	1
Do you consider you are well?			
Improved	4	4	99
Unimproved	25	15	9
Unimproved	1	8	2

tion will be productive of even better results in the future.

### SUMMARY AND CONCLUSIONS

It appears that the selection of operation for benign prostatic hypertrophy must depend on the experience and technical skill of the individual surgeon. It is probably true that in equally skillful hands the suprapubic operation carries a higher mortality than do the other methods, and that the perineal and transurethral operations have a comparable mortality.

All three operations when skillfully performed can be expected to produce excellent results, although in my hands the transurethral operation shows to advantage over suprapubic prostatectomy. Urinary incontinence and rectal injury which occasionally complicate perineal prostatectomy even in the most skillful hands, are not to be expected in either the suprapubic or the transurethral operation.

From the standpoint of the patient properly performed transurethral resection shows to advantage over the open methods of prostatectomy in those factors of comparison which interest him that is, he has a more comfortable and more am-

bulatory postoperative period, his period of hospitalization is less, and his functional results are at least as good.

It is my opinion that the advantages of transurethral prostatectomy make it the operation of choice for benign hypertrophy, whenever it can be properly performed. I believe that the size of a benign gland does not constitute a criterion for or against resection except in relation to the skill and dexterity of the individual surgeon. The accomplished resectionist must recognize his own limitations and select the operation with a full and honest recognition of those limitations. Transurethral resection has a place in the armamentarium of every urologist; the degree of its usefulness, like that of the other methods of prostatectomy, depends on the skill and judgment with which it is employed.

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### DISCUSSION

DR. FLETCHER H. COLBY, Boston: Transurethral resection has been severely and unfairly criticized but in spite of its opponents the operation has become a recognized surgical procedure. Discussions once directed against the operation itself are now chiefly concerned with its indications. What varieties of prostatic obstruction are best relieved by transurethral resection? When the widest differences of opinion regarding the indications for this operation exist among urologists, what must be the uncertainty of the physician seeking to advise his patient?

A pertinent communication by Foley on this subject appeared recently in the *Journal of Urology* (43:565-571, 1940) under the unusual title, "The Present Status of Transurethral Resectionists, Competent and Otherwise." He writes:

Statements concerning the present status of prostatic resection by urologic surgeons of truly great renown have produced perfectly fatuous and at times acrimonious differences of opinion which are meaningless. In one article is found the assertion that prostatic resection is a dangerous and worthless procedure which never should be employed beyond the original scope of Young's punch operation. It may be presumed that this author knew more about his own skill, ability and experience in resection than anyone else and that in respect to these he made a good appraisal. In another article it is said that in all cases resection is vastly superior to any form of open operation and should be employed in all cases of vesical neck obstruction. If this writer knows accurately his skill and ability and has profited by his experience, he is unique. These authors are not talking about the same thing. They are not talking about the present status of transurethral resection. There is no such thing. They are speaking of the status of resectionists and usually of their own status as such.

supervision, they organized their sons, forty-six in all, into a team and supervised their play throughout the season, during which thirteen games were played. The average weight of the boys was 80 pounds. No play of any sort was allowed without some of the elders being present. Careful investigation shows that aside from a few minor contusions and an occasional traumatic epistaxis no injuries occurred. Part of this success was also due to the "quick whistle," which goes far toward preventing injuries.

From the reports given above it is only fair to conclude that the supervised game has received all the help it can expect from the rules, equipment, playing conditions, officials and the medical selection of participants. The severity of the injuries can, however, be materially controlled by the elimination of players who have been injured during a game or who have become overfatigued. It should be the duty of the doctor at the game to see to it that all such players are promptly removed. Absolute adherence to this policy will provide the best safety factor for minimizing the hazards of the future.

The number of injuries sustained in organized play contrasts sharply with the number received by boys who play on the streets, in vacant lots and backyards, in parks and so forth. These boys when injured are usually unable to receive medical care on the spot and as a result seek aid from the nearest hospital. Judging from the records of the Boston City Hospital, the conditions created by this situation have become worse each year for the last few years. Over the week ends from late September until early December it is customary to treat from twenty-five to thirty boys in the accident ward of the Boston City Hospital for football injuries alone. On Monday mornings during this period an average of thirty-five to fifty players are treated in the Out-Patient Department. Although a great many of the patients have no fracture, they have at least sufficient trauma to warrant an x-ray examination. The headmaster of a Boston high school recently stated that he is constantly having absentees on Monday morning, or receiving requests from boys for permission to go to their doctors, or more often to hospitals, to seek relief from injuries incurred over the week end, particularly on Sundays. He added that these boys play in scrub games and are not connected with any organized group.

Several years ago one of the coaches of one of the largest high schools in Boston wrote as follows:

We had no injuries during the season except a few muscle bruises, and according to the report of our

truant officer, no member of the squad was absent from school on account of any injury received from football. We did, however, have seven fractures and dislocations from boys playing sand lot or backyard football. These boys, however, were not members of the high school squad.

The injuries sustained by boys who came to the Boston City Hospital in the fall of 1939 for treatment are listed in Table 4. Two boys were ad-

TABLE 4 *Football Injuries Sustained by Boys Seen at the Boston City Hospital, 1939*

Type	No. of Cases
Ruptured spleen (splenectomy)	1
Fractures	22
Clavicle	6
Both bones of forearm	2
Wrist	2
Lower end of humerus	1
Olecranon	1
Patella (open reduction)	1
Tibia	1
Fibula	2
Both bones of leg	3
Pott's	1
Ankle (tri malleolar)	1
Ischium	1
Concussion	1
Dislocated shoulder	1
Acromioclavicular separation	1
Dislocated elbow with fractured medial epicondyle (open reduction)	1
Contusion of crest of ilium (severe)	1
Synovitis of knee (crutches used)	1

mitted and treated for fractures of the cervical spine, but x-ray examination failed to reveal a fracture. In addition to these injuries, there were a countless number of sprains, contusions and lacerated wounds, most of which required x-ray examination for diagnosis. A great many of these cases called for hospital care.

From what has been said, it is evident that the worst injuries are to be found in unorganized groups. This type of play is unsafe, produces serious injuries and gives football an unjustified reputation as a dangerous game. The boys play under the most adverse conditions without supervision, without officials, with no medical care or selection of players, and usually without protective equipment of any sort. They play on the bare ground, sometimes on pavements, and often on dusty fields, and without regard to the matter of fatigue. In the absence of officials, the boys are subjected to treatment that is against the rules, namely, clipping, piling, the illegal use of hands, holding, slugging and unnecessary roughness. Proper supervision would do away with most of these practices.

Many of the accidents mentioned occur following minor injuries, after which boys continue to play just because they can "take it." It has long been my custom to remove from the game all

boys who limp because of a knee injury no matter how trivial. In this way the incidence of "schoolboys' knee" has been decidedly reduced. The commonest sequelae among athletes is the "trick knee", this is usually due not to the original trauma but to a second blow received in the same game, or in a subsequent one to which the player has been admitted too soon after injury.

Much of the trouble results from adherence to the spirit of play, a practice criticized in an editorial in the January 2, 1932 issue of the *Journal of the American Medical Association* which, in part, reads as follows:

Even in war humanity protests against the return of men to the front until they have recovered from their wounds. How often is a limping football player returned to the play with an encouraging and admonishing slap on the back by the coach who "needs him" in the game. In everyday life, even slight injuries are given full opportunity to be repaired. The modern football crowd shrinks for the injured players to "stuck it out."

It is this sort of practice that has often caused some of the serious accidents to boys who are not physically prepared to take care of themselves. Another cause of injury is the boys' utter lack of knowledge of one of the fundamentals of football, namely, the art of blocking and tackling.

It is to this unorganized group that all those interested in physical education and athletics should turn their attention in the future. Parent teacher associations, boys clubs, athletic officials, Boy Scout leaders, playground supervisors, grammar and high school teachers, coaches and, lastly but by no means least, parents, can all help in eliminating these serious conditions by a campaign of education and helpful advice. Young America will play football, with or without helpful supervision, so that it is the duty of their elders to help regulate the playing of juveniles.

#### SUMMARY

Under proper supervision, with adequate equipment, with games played on good fields, with a doctor present to supervise all injured players, with properly arranged schedules, with due regard for extreme weather conditions and with competent officials in charge of games, football is certainly worth while. The results obtained in properly organized and supervised groups as compared with those in unregulated ones, show that the incidence of football injuries can be reduced to an extremely low figure.

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### TREATMENT OF SYDENHAM'S CHOREA BY FEVER AND VITAMIN B THERAPY\*

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**S**YDENHAM'S chorea, or chorea minor is an encephalopathy of indefinite etiology, occurring usually in young persons, most commonly between the ages of five and fifteen. It is manifested by numerous involuntary movements of the entire body inco-ordination, diminished muscle tone and emotional and behavior disturbances of varying severity. While the exact cause of the condition is still unknown the frequent concurrence of rheumatic fever and endocarditis with chorea and the fact that a number of cases are preceded by scarlet fever, suggest a streptococcus as a possible causative organism. There are probably other factors in the etiology besides an infecting organism, such as dietary deficiencies, emotional strain and a basically unstable nervous

system. The disease is usually self limited, as most mild cases terminate in four to ten weeks, more severe cases may last three to six months, while some children when closely observed continue to display numerous choreiform movements for years after the acute attack. Some of these cases are diagnosed as *maladie des tics* and are considered to be of psychogenic origin. A more careful review of the past history of the patient however, will occasionally disclose that it began as a severe chorea which somewhat improved, with some of the movements gradually acquiring the character of tics. The association with emotional factors in etiology therefore should not in itself rule out chorea as a cause.

#### HISTORICAL ASPECTS OF TREATMENT

Sydenham was the first to give us a clear description of the disease and the first to outline the treatment for this condition. Its name *chorea*

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vise the patient and the machine, and the need for hospitalization for two weeks to a month for the treatment

#### FEVER THERAPY AND VITAMIN B THERAPY

In view of the frequency of cardiac changes in chorea and the fear of untoward complications following eight hours' exposure of a child to a temperature of 104°F or over, as recommended by Neymann and his associates, I believed that reduction in the time the patient was exposed to the high fever would be worth attempting, and to offset the reduction increased the number of treatments if necessary. At the same time the factor of vitamin B deficiency was also considered as a possible contributing cause in the development of cardiac involvement and the hyperirritability of the nervous system. The patient's diet was therefore complemented by the addition of vitamin B complex\* given orally, and in some cases thiamin chloride was also given intravenously.

In the last three years I have treated 20 children suffering from chorea in various degrees of severity. Some of them were seen in a mental hygiene clinic, where they were brought because of various behavior disturbances and apparent clumsiness. A small number were referred to a crippled children's clinic when the presence of encephalitis was suspected. Seven patients exhibited all the signs of very severe chorea, as manifested in continuous movement of the face and extremities, inability to feed or dress themselves, hypotonia and muscle weakness, and inability to walk without support. The other 13 patients presented moderately severe or mild forms of the disease. In some cases they had been first referred by the school nurse or teacher because of emotional instability or clumsiness, and in a few they were said to have made faces at their teachers and fellow students. The presence of chorea was usually discovered during the physical examination. A number of patients in this group gave a history of an attack of severe chorea three months to two years previously, from which they had apparently never completely recovered.

My method of treatment for severe cases—an advanced cardiac condition was not found to be a contraindication to the treatment—consists in giving the patient six or seven fever treatments once every three or four days, and maintaining the temperature at 104°F or over for about two

hours. Every treatment is followed by the injection of 10 to 15 mg of thiamin chloride intravenously shortly after removal from the fever cabinet, while the temperature still remains elevated. The patients also receive 4 to 8 cc of vitamin B complex orally three times daily.

Five of the 7 very severe cases received fever therapy. In 1 the temperature was raised by means of diathermy, and the other 4 received inductothermy fever. The first patient received a total of ten hours of diathermy fever of over 102°F in ten treatments, with complete cessation of symptoms at the end of the fever therapy. In the inductothermy-treated group, the patients received six or seven fever treatments, with two or three hours of fever of over 104°F at each treatment, or about twenty-one hours of fever of over 102°F. I usually try to maintain the patient's temperature between 104 and 105°F for about two hours, and he is kept about four or five hours in the fever cabinet during each treatment. The results in this group have been excellent, for the movements have disappeared entirely by the end of the treatments and there have been no recurrences so far.

In a case of extremely severe chorea, complete cessation of symptoms resulted after four intravenous injections of 10 mg of thiamin chloride at bi-weekly intervals, and 8 cc of vitamin B complex orally three times daily for the same period. In a less severe case of three years' duration, where the symptoms did not respond well to oral therapy, four weekly intravenous injections of 10 mg of thiamin chloride, reduced the choreiform movements to a minimum and also brought marked amelioration in enuresis of long standing.

In the moderately severe and mild cases hospitalization was not found necessary. In a few cases discontinuation of school for a short period was advised, especially where the child's impulsiveness, irritability and sometimes mild paranoid attitude toward the teacher and other students made it worth while to keep the child temporarily away from school while he received psychiatric attention. When his condition was explained to the teacher, special arrangements were made not to overexert the patient and to discharge him from school earlier than the usual time. This group of patients received vitamin B complex orally, usually 4 to 8 cc three times daily, in several cases supplemented by other vitamins. The improvement was less spectacular than in the fever-treated group, but the changes for the better in the behavior of the youngsters became evident in a few days after medication had been begun. Irritability was lessened, assaultiveness disappeared

\*Each teaspoonful of the vitamin B complex contained the following: thiamin chloride (vitamin B<sub>1</sub>) 1.5 mg, riboflavin (vitamin B<sub>2</sub>) 0.6 mg, dermatitis factor (vitamin B<sub>6</sub>) approximately 20 rat-day units, filtrate factors approximately 20 rat growth units, nicotinic acid equivalent to 25 gm of whole liver.

and a state of contentment replaced the previous aggression and surliness. The improvement in the psychic sphere paralleled the changes for the better in physical condition. Usually by the end of a month most of the symptoms had disappeared.

### REPORT OF CASES

The following patient was the first to receive diathermy treatment. She had a mild psychotic state associated with ideas of persecution a threatening attitude and periods of assaultiveness. She responded well to treatment, and although she nearly recovered after the fifth treatment she was given five more in order to prevent a recurrence.

**CASE 1** A 13-year-old Polish-American girl was admitted to the New Hampshire State Hospital on January 24, 1937, because of marked inco-ordination of extremities, speech disturbances and period of irritability and assaultiveness. Two years previously she had swelling of the joints, associated with fever. A year later she had an attack of "acute chorea" and was confined to the county hospital for 5 weeks when she ran away in an unimproved condition. For the last month previous to admission her movements became markedly worse. She expressed ideas of persecution and threatened her brother with a jackknife.

Physical examination showed marked inco-ordination of the hands, choreiform movements of the face and extremities, inability to keep the tongue protruded and a systolic murmur at the apex transmitted to the axilla and the entire precordium with an apex impulse in the 6th interspace, 2.5 cm. outside the midclavicular line. The pulse was 112. The biceps, triceps, knee and ankle jerks were exaggerated.

The patient received ten diathermy treatments with a total fever of over 102° F. for 10 hours. She was given 8 gm. of Vegex three times daily and cod-liver oil. At the end of the fourth treatment her movements were greatly reduced, and they had nearly disappeared by the end of the sixth treatment. The mental symptoms and behavior difficulties also improved and she was discharged on April 10 as recovered. There has been no recurrence of symptoms.

The next patient reported was referred with a possible diagnosis of postencephalitic state. The rapid and complete recovery with fever therapy placed her definitely in the chorea group.

**CASE 2** A 7-year-old Albanian American girl was first seen in March, 1939 at the Concord Mental Hygiene Clinic because of poor physical condition, continuous movement of the extremities and face, incoherent speech and inability to stand up or walk without support. She required constant attention as she could neither feed nor dress herself. Physical examination at this time the patient was very pale, malnourished and unable to stand without support. She was in a continuous state of motion, the movements involving the face, abdomen and extremities. The pupils were dilated. There was bilateral hippus, the disks were congested and the fundal veins were congested. The patient was unable to keep the tongue protruded and co-

ordination was very poor. The tonsils were enlarged and cryptic. The reflexes were markedly increased. The knee jerks were exaggerated but the other reflexes were normal.

The laboratory findings were normal except for a moderate leukocytosis and an increase in the blood sedimentation rate.

On May 23 the patient was admitted to the Elliot Hospital for fever therapy. She received six inductothermy treatments for a total of 14 hours of fever above 104° F., with a maximum temperature of 105°. She also received 10 mg. of thiamin chloride intramuscularly following the fever treatments and 4 to 8 cc. of vitamin B complex three times daily. By the completion of the fever treatment, 3 weeks after admission the sedimentation rate had dropped to normal. The patient gained 4 pounds and all her choreic symptoms disappeared. She was able to feed and dress herself and her gait appeared normal. After a tonsillectomy had been performed she was discharged 1 month after admission as recovered. There has been no recurrence of symptoms.

**CASE 3** An 8-year-old girl was seen first on June 13, 1939 in the Crippled Children's Clinic at the Balch Hospital in Manchester, New Hampshire, for inco-ordination, inability to stand without support or dress or feed herself, continuous movements of the face and extremities and explosive, unintelligible speech. Symptoms first appeared in April, 1939 following appendectomy and had been getting worse.

Physical examination showed a very pale girl in continuous motion. Sides had to be placed on her bed to keep her from falling out. The disks were clearly outlined and the fundal veins were congested. There were continuous twitchings of the face, marked tremor of the eyelids, inability to keep the tongue protruded and inco-ordination of the extremities. The deep reflexes were greatly increased. There was a systolic murmur at the apex, transmitted to the axilla. The tonsils were enlarged and infected.

The laboratory findings were normal.

The patient received six fever treatments at 4 or 5-day intervals, 10 mg. of thiamin chloride following the fever treatment and 8 cc. of vitamin B complex three times daily. At the end of the third treatment her movements were greatly reduced, and they disappeared at the time of her discharge on July 21. A tonsillectomy was performed during her stay in the hospital. She received 7 hours of fever of over 104° F., with a maximum of 105° F. and 14 hours over 102° F. There has been no recurrence and she was attending school at the last report.

**CASE 4** A 13-year-old boy was admitted to the Elliot Hospital on July 5, 1939 with a diagnosis of Sydenham's chorea and rheumatic endocarditis. In April he had developed a sore throat and following that pain in the joints. In June marked choreic symptoms had appeared. He had been in bed since April.

Physical examination showed a pale boy with continuous movements of the face and extremities. His speech was very indistinct. The optic disks appeared pale especially the right. The pupils were dilated, and reacted to light and distance. There was bilateral hippus. There were continuous spasmodic movements of the facial muscles and the patient was unable to keep the tongue protruded. The hands were choreic in shape. Co-ordination was very poor. The patient was unable to feed himself or sit up without support and required side boards on his bed. The extremities were cold and moist. The biceps, triceps, knee and ankle jerks were slightly exaggerated.

vise the patient and the machine, and the need for hospitalization for two weeks to a month for the treatment

### FEVER THERAPY AND VITAMIN B THERAPY

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hours. Every treatment is followed by the injection of 10 to 15 mg of thiamin chloride intravenously shortly after removal from the fever cabinet, while the temperature still remains elevated. The patients also receive 4 to 8 cc of vitamin B complex orally three times daily.

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Nursing Association on November 21, 1939 for numerous involuntary movements of body dropping things, and poor schoolwork. She had always been in good health until August, 1939 when she displayed numerous abnormal movements involving the face, hands and legs. She complained of being dizzy at times, could not dress her self dropped spoons and dishes and was unable to turn the pages of her books while at school. She improved slightly under sedatives. She was irritable at home, given to temper tantrums, appeared very clumsy in handling things and continued to be fidgety and restless.

Physical examination showed a restless patient who was unable to sit still. There was a marked flutter of the eyelids. The fundi and pupillary reactions appeared normal. The patient was unable to keep her tongue protruded. There was marked inco-ordination in the hands when trying to button clothes or turn pages. The grasp was unsteady and the hands were athetoid. The reflexes were increased.

The patient was given 4 to 8 cc. of vitamin B complex three times daily and within 3 weeks the co-ordination improved. She appeared much more stable emotionally and as described by the mother was "like her old self again."

#### DISCUSSION

That streptococcal infection is not alone responsible for the symptoms of rheumatic fever and chorea has been suspected by many observers. The added factor of metabolic disturbances in the etiology of chorea and rheumatism in children either due directly to food deficiency or to inability to metabolize certain protective substances in the diet, should be given further consideration. The kinetic disturbances and the emotional instabilities in chorea are possibly akin in origin to the kinetic and psychic states seen in alcoholic deficiency states, namely delirium tremens and Korsakoff's psychosis. While it was assumed in the past that the toxic influence of alcohol was responsible for the abnormal phenomena of the nervous system it is now nearly certain that it is food deficiency or the inability of the alcoholic patient's stomach to absorb vitamin B components from the diet, that accounts for such changes. This premise prompted the use of vitamin B complex as a complement to the diet in the treatment of chorea.

The action of fever on chorea is probably non-specific, and is similar to its action on arthritis, asthma and other conditions. It produces general capillary dilatation, reduces vasospasm in the joints and small cerebral blood vessels, improves the flow of blood, increases the number of circulating red blood corpuscles in the blood stream, greatly improves oxygenation and accelerates the supply of oxygen to all parts of the brain, besides probably also assisting in mobilization of all the defense mechanisms of the body. Artificial fever however if continued too long defeats its own purpose for it then produces vasomotor paralysis and cia-

nosis rather than increased oxygenation. It is this that prompted me to reduce the number of bouts of fever given to patients, with equally successful results. None of the patients had any untoward reactions during the fever treatments or following the intravenous medication. The administration of thiamin chloride during the stage of capillary dilatation and improved circulation helped to produce better diffusion of the medication throughout the central nervous system. The patients required no other medication during their stay in the hospital or at home.

Osler<sup>1</sup> in his excellent monograph on chorea states, "Psychical disturbance is rarely absent in chorea fortunately in the majority of the cases it is slight in degree." He lists the following outstanding symptoms: disturbance of the moral sense, perverseness, great irritability of temper, with emotional outbreaks and change in character, disturbances in the faculties of memory and attention, transient loss of power to read and write, and impulsive actions. It is probable that some of the behavior disturbances occurring in children at an older age are sequelae to an attack of chorea which was either so mild in its physical characteristics as not to attract attention or was not brought out in the past history. Shaskan,<sup>22</sup> in a recent study of a number of choreic children with behavior disturbances at Bellevue Hospital, New York City, concluded after interviewing many of the parents that personality factors are not the cause of the affection as believed by some observers, and that in most cases no significant disclosures concerning behavior, personality of the children and family history were obtained which would support such an assumption. The improvement in behavior after treatment he believed to be of additional significance. The changes for the better in the personalities and general behavior of the children with chorea whom we treated tend to support Shaskan's viewpoint. The changes were observed both by the parents and the teachers. The behavior changed for the better although the home and school environment remained unaltered.

#### SUMMARY AND CONCLUSIONS

Twenty patients with severe, moderately severe and mild cases of Sydenham's chorea were treated. Five of the 7 severe cases received artificial fever therapy together with vitamin B complex given orally and thiamin chloride given parenterally. One severe and 1 moderately severe case received thiamin chloride parenterally and vitamin B complex orally, while all the others received oral medication only.

In the electropyrexia-treated cases recovery was



produced with about fourteen hours of fever at 104°F or over. When this was combined with vitamin B therapy, advanced cardiac conditions were found to be no contraindication to the fever treatment. Usually a change for the better in the cardiac status was noted at the end of the treatment.

One of the 2 cases treated with thiamin chloride responded with cessation of symptoms after the second intravenous injection of 10 mg of the drug.

Various degrees of behavior disturbances were seen in most of the moderately severe and milder cases. They all received 4 to 8 cc of vitamin B complex orally, three times daily. The improvement in physical manifestations was less rapid than it was in the fever-treated cases, but most of the symptoms disappeared within one month. No hospitalization was required for any patients in this group. Improvement was noted in their behavior concomitantly with the change for the better in the choreic manifestations.

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## NEW HAMPSHIRE MEDICAL SOCIETY

### PROCEEDINGS OF THE ONE HUNDRED AND FORTY-NINTH ANNIVERSARY

MAY 14 AND 15, 1940

TUESDAY MORNING, MAY 14

THE members convened in the Hotel Carpenter, Manchester, at nine-thirty o'clock.

The first part of the morning was devoted to the following round-table conferences:

- MEDICINE Bronchial Asthma — Leader, Philip B Daniels, Keene.
- SURGERY Surgical Diseases of the Gall Bladder — Leader Herbert B Messinger, Franklin
- NOSE AND THROAT Common Diseases of the Ear, Nose and Throat — Leader, Henry H Amsden, Concord
- OBSTETRICS Postpartum Hemorrhage — Leader, Marion Fairfield, Nashua.

During the second half of the morning the following round-table conferences were held:

- MEDICINE Endocrinology — Leader, J Dunbar Shields, Concord
- SURGERY The Management of Head Injuries — Leaders, M Dawson Tyson and John B McKenna, Hanover
- UROLOGY Injuries to the Kidney — Leader, Isadore J Zimmerman, Manchester

ORTHOPEDICS Fractures — Leader, Harris E Powers, Manchester

TUESDAY AFTERNOON, MAY 14

The session convened at two o'clock with President Woodman presiding.

The early part of the session was devoted to a symposium on diabetes with the following titles and speakers: "Diet and Insulin," Dr Alexander Marble, Boston, "Diabetes in Children and Adolescents Problems and management Pregnancy in the Diabetic," Priscilla White, Boston, "Diabetic Hazards and How to Meet Them," Dr Elliott P Joslin, Boston.

The symposium was followed by an address, "The Medical and Surgical Management of Ulcerative Colitis," by Dr More Mills, of New York City.

WEDNESDAY MORNING, MAY 15

The first period beginning at nine-thirty o'clock was devoted to the following round-table conferences:

**MEDICINE.** Hypertension. — Leader, Jeremiah J. Morin  
Rochester

**SURGERY.** The Treatment of Burns. — Leader Rad-  
ford C. Tanzer Hanover

**PEDIATRICS.** Infant Feeding — Leader Thomas B.  
Walker Portsmouth.

**SKIN.** Certain Problems in Syphilis. — Leader Henry  
W. N. Bennett, Manchester

The general session convened at eleven o'clock.

**PRESIDENT WOODMAN** My first duty on this morning's program is always a pleasant one namely, to introduce the delegates from the Societies of the New England States.

I shall first call on Dr. William T. Rowe, of Rumford, Maine.

**DR. ROWE** The Maine Medical Association extends its best wishes to the members of the New Hampshire Medical Society.

I extend an invitation to the members to attend our meeting, which takes place at Rangeley Lakes, June 23, 24 and 25. If you do not like medical papers, we shall have good fishing and golf for you. We want to see as many of you up there as can come.

**PRESIDENT WOODMAN** If Dr. Albert M. Cram of Vermont is here we should like to have a few words from him. [Dr. Cram was not present in the auditorium.]

We shall now hear a few words from Dr. Charles S. Benson of Haverhill, Massachusetts.

**DR. BENSON** I am very glad to come up here and give you greetings from the Massachusetts Medical Society. I am no stranger. For at least a decade I have been attending your meetings.

The Massachusetts Medical Society has its meeting next week in Boston. Our society extends its best wishes and an invitation to all who desire and would like to visit the meetings which will be held at the Copley Plaza on Tuesday and Wednesday.

**PRESIDENT WOODMAN** Another delegate from Massachusetts is Dr. Edward A. Adams, of Fitchburg.

**DR. ADAMS** I second the invitation which Dr. Benson has given and I also wish to say that I have had a very fine time here. Your medical meetings are most valuable, and I have heard some excellent papers. The round-table conferences on burns and head injuries were very fine. But the nicest thing of all is meeting new friends and seeing old friends whom I met last year.

**PRESIDENT WOODMAN** I now call on our old friend Dr. Karl T. Phillips, of Putnam, Connecticut.

**DR. PHILLIPS** The Connecticut State Medical Society sends its best wishes to your society. I am sorry that our meeting comes at the time of the meeting in Massachusetts, but you have your choice. The Connecticut meeting will be held next Wednesday and Thursday, at the Hotel Bond. We also have tentative plans for an excellent meeting in the fall, the Clinical Congress.

I must admit that I have had a better time up here than I usually do at the Connecticut meetings, and I guess that speaks for itself.

**PRESIDENT WOODMAN** I now have the very great pleasure of introducing a man who is at the top. When you consider the comparative efforts, strength and virtue of the American Medical Association, as compared with any other medical society in the world, you will realize that Dr. Van Etten is actually "tops."

It gives me great pleasure to introduce to you Dr. Nathan B. Van Etten, president-elect of the American Medical Association.

There followed an address, "Education of the Intern," by Dr. Nathan B. Van Etten, president-elect of the American Medical Association, and Dr. Nathan Smith of New York City.

#### WEDNESDAY AFTERNOON MAY 15

The session convened at two o'clock, with Vice-President Ezra A. Jones presiding.

**CHAIRMAN JONES** First, on this afternoon's program is the presentation of the medals to those who have been members of the Society for fifty years.

Dr. Woodman had planned to say what is written here. After looking it over, I decided I could not say anything half so well, so I am going to read what he has written.

It is now my duty and very great pleasure to recognize on behalf of the New Hampshire Medical Society these distinguished men who are members of the Society.

These men have served their fellow-men as physicians and they have been members of the Society for fifty years. They have been integral parts of much that has been accomplished in medicine during the past half century. They have risen to their daily tasks each day and discharged them faithfully and well. Through fair weather and bad weather, through good times and bad times, through the vicissitudes of life they have carried on.

Therefore, it is fitting that at this great milestone the Society should honor them by the presentation of these tokens of our esteem.

In accepting these beautiful medals may you enjoy not only their beauty of design and fine materials but also the esteem, appreciation and honor which it is our privilege to bestow.

fapyridine alone in the pneumonias of adults<sup>2-24</sup> includes 2052 cases with 162 deaths, a mortality of 7.9 per cent

A second group comprises the reports of authors who used both serum and sulfapyridine in adults<sup>25-42</sup>. It includes 2224 cases treated with specific serums alone, with 301 deaths (13.5 per cent), 2638 cases treated with sulfapyridine alone with 256 deaths (9.7 per cent), and 557 cases treated with the combination of serum and sulfapyridine, with 95 deaths (17.1 per cent). The combined therapy was reserved mostly for the severest cases or for those in which the drug did not bring about a satisfactory result.

A third group of reports by other authors, dealing solely with the use of specific serums<sup>43-53</sup> just prior to or during the first few months after the introduction of sulfapyridine, includes 2727 cases with 263 deaths (9.6 per cent). The latter results reflect the remarkable improvements in serotherapy brought about by the introduction of therapeutic rabbit serums. Nevertheless, they still represent a more limited group of cases of pneumonia, and in that respect the results are not strictly comparable with those obtained with chemicals.

The fourth group of reports deals with the treatment of pneumonia in infants and children. This includes 1542 cases treated with sulfapyridine alone<sup>24, 25, 31, 35, 54-73</sup> with 46 deaths (3.0 per cent), and a more limited group of 312 cases<sup>35, 68, 74-76</sup> treated with serum among which there were 11 deaths (3.5 per cent). Of interest is the fact that a large proportion of the latter cases were given serum intramuscularly. Among the sulfapyridine-treated cases there were 70 in which the pneumonia complicated pertussis, and 12 (1.7 per cent) of these patients died.

Essentially, these results substantiate the conclusion drawn from the earlier reports. All authors emphasize the dramatic clinical response so regularly observed in uncomplicated cases, particularly in young adults. Pediatricians are particularly enthusiastic because of the ease of administration of the drugs, as compared with the difficulties encountered when serums are used. The deaths that are still encountered occur mainly in very old persons, in patients with complicating severe systemic disease and in those in whom treatment is delayed until the patient is already moribund, or until focal infections have already become established. The discrepancies in the mortality among the individual reports are attributable in large measure to the differences in the frequency with which these factors are encountered.

Another source of discrepancy depends on the diagnostic criteria used by various authors. Lobar

and bronchopneumonias, primary and secondary pneumonias are considered together by some and separately by others. Most authors have tried to limit their reports to cases in which pneumococci were identified in sputum or other body fluids. Of course, the relation of the pneumococci to the disease is not always clear, particularly when "higher" types are identified solely from sputum or throat cultures.

It is not possible to determine from the available data the true value of the drugs in non-pneumococcal pneumonias, owing in large part to the difficulties in arriving at an etiologic diagnosis. The application of the Neufeld method of typing directly from sputum has given most laboratory workers a feeling of unjustified sufficiency. Reports of "no pneumococci" or "pneumococci, no type" are only too frequently based on cursory inspection of wet preparations of sputum with diagnostic rabbit serum. Attempts are rarely made to classify the predominant pathogenic organisms by morphological and cultural methods.

The most striking and most constant beneficial effects from sulfapyridine have occurred in the cases of primary pneumococcal pneumonia. So far as can be determined from available reports, the results in cases of bronchopneumonia and in secondary pneumonias have also been good, but usually not so striking. The effects in pneumonias due to hemolytic streptococci are usually favorable, but not so dramatic as in those due to pneumococci. Only occasional favorable results are noted in staphylococcal pneumonias, while the results in cases of Friedlander's bacillus pneumonia have been, on the whole, discouraging.

No important new facts have been brought out concerning the toxicity of sulfapyridine. Most writers stress the relative ease of administration, especially in children, and the rarity with which serious complications of treatment are encountered if the usual simple precautions are followed. The importance of ensuring adequate fluid intake and output to prevent the significant renal complications is stressed. Since prolonged therapy is not necessary except where focal complications are being treated, serious granulocytopenias are not frequent. When therapy is continued for more than one week, frequent white-blood-cell counts and blood smears should be made, and the drug stopped as soon as leukopenia with reduction of polymorphonuclear cells is detected. It is also becoming evident that the conditions under which the drug is contraindicated are very rare. Extreme caution, however, must be used if the drug is given in the presence of renal disease associated with nitrogen retention, in hepatic disease, to pri-



been fully substantiated by these reports and by our own observations. There is now very little excuse for using sulfanilamide in the treatment of any acute pulmonary infection, except where it is impossible to use sulfapyridine (or sulfathiazole) or, perhaps, in cases caused by hemolytic streptococci.

#### SULFATHIAZOLE

Many sulfonamide derivatives have been synthesized and studied in the hope of obtaining compounds with greater antibacterial action and less toxicity than those of sulfapyridine. One that has given sufficient promise to warrant extensive clinical trials is sulfathiazole. This compound, together with some closely related ones, was synthesized by Fosbinder and Walter<sup>89</sup> and found to be active against experimental hemolytic streptococcal and pneumococcal infections in mice. Further laboratory studies have indicated that sulfathiazole may be less toxic than sulfapyridine when used in therapeutic doses,<sup>90</sup> and that it is usually as effective as or slightly more effective than the latter *in vitro*<sup>91-93</sup> and in infections of animals with staphylococci, hemolytic streptococci and pneumococci.<sup>94-99</sup> Clinical reports suggest that it may be useful in the treatment of staphylococcal infections, in pneumonia, in infections of the urinary tract and possibly in a number of other infections.<sup>85 100-107</sup>

Sulfathiazole is absorbed and excreted more rapidly than is sulfapyridine, and less of the former appears in the blood and urine in the acetylated form. Although somewhat more soluble than sulfapyridine, it is still quite insoluble and must be given orally or, in the form of the sodium salt, intravenously. It is not absorbed well after rectal administration, even when given as the sodium salt. While it is distributed throughout the body in about the same manner as sulfapyridine, it does not penetrate as well into the brain and spinal fluid, and therefore should not be used in the treatment of meningitis.<sup>84 104 108-110</sup>

Although numerous clinical studies of the use of this drug have been carried out during the past few months, only a limited number of published reports were available at this writing. From these, and from our experience at the Boston City Hospital, it would appear that its chief advantage over sulfapyridine, from the point of view of toxicity, is that nausea and vomiting are less frequent and considerably less severe. Anemia is less frequent and leukopenia is probably as common. Agranulocytosis occurred after three weeks of treatment with sulfathiazole, and was the cause of death in one of our patients with subacute bacterial endo-

carditis. Long, thin crystals of the drug are frequently seen in clusters, like sheaves of wheat, in microscopic examination of the urine. Renal complications similar to those observed under sulfapyridine therapy have been reported.<sup>111-113</sup> They probably occur somewhat less frequently, but may be fatal. Drug fevers and rashes are probably more frequent than with sulfanilamide or sulfapyridine. A peculiar type of dermatitis simulating erythema nodosum has been observed, the raised red nodules occurring mostly around the knees and elbows. In addition, conjunctival lesions and an erysipeloid appearance of the malar region and lower lids have been noted.

Sulfamethylthiazole has therapeutic effects similar to those of sulfathiazole. It is much less soluble and is probably more toxic. Its clinical trial has been discontinued owing to the occurrence of cases of severe peripheral neuritis from its use.

In the treatment of pneumonia, both in adults and in children, the results obtained with sulfathiazole have been comparable to or slightly better than those obtained with sulfapyridine.<sup>85 109 110 114</sup> The clinical response, as indicated by the subsidence of fever, is said to be somewhat more delayed. The better results may be due largely to the fact that there is less nausea and vomiting. The same dosage in adults may be employed for both sulfapyridine and sulfathiazole, namely, an initial dose of 2 gm, repeated in two hours and followed by 1 gm every four hours, day and night, until three or four days after the temperature reaches normal. Some physicians prefer to use a larger initial dose (3 to 5 gm) or to give 1 gm every three hours, but neither dose is necessary except in very severe cases. On the same dosage, the blood levels tend to be somewhat lower with sulfathiazole than with sulfapyridine. Sulfathiazole has now been released for sale under the provisions of the recent Food, Drug and Cosmetic Act.

#### BACTERIOLOGY AND IMMUNOLOGY

Mention may be made here of a number of recent studies which are of interest and may be of practical significance in relation to chemotherapy and serotherapy of pneumococcal infections.

##### *Effect of Sulfapyridine on the Pneumococcus Capsule*

In the early studies on sulfapyridine, Whitby<sup>115</sup> noted degenerative changes in the capsules of pneumococci obtained from experimentally infected mice undergoing treatment with this drug. Telling and Oliver<sup>116</sup> and Lawrence<sup>117</sup> noted that pneumococci in the sputum of sulfapyridine-treated pa-

uents lost the property of swelling with homologous type specific rabbit serum. This suggested that the drug might act directly on the organisms causing degeneration of the capsule, thus rendering them avirulent and readily susceptible to phagocytosis. From the point of view of the etiologic diagnosis of pneumonia this seemed to explain the frequent failures to obtain satisfactory typing from sputum collected after the institution of drug therapy. Further extensive observations in many laboratories, however, failed to substantiate this idea.<sup>20, 118-120</sup> It is more reasonable to assume that the difficulties in the typing of sputum from drug-treated patients are the result of a decline in the number of the susceptible encapsulated pneumococci, and that this, in turn, is due to the bacteriostatic and bactericidal action of the drug. The finding of large numbers of such encapsulated organisms in the sputum following chemotherapy may be taken as good evidence either that the drug failed to act on that particular strain or that the treatment was inadequate. The latter is the more frequent explanation.

### *Sputum Studies*

Frisch<sup>122</sup> found that the numbers of extracellular encapsulated pneumococci seen in ordinary stained smears of fresh rusty sputum from pneumonia patients may serve as a guide for prognosis. The larger the number of free pneumococci, the worse is the prognosis. Following treatment with sulfanilamide, he found a rapid decline in the number of pneumococci during twenty-four to thirty-six hours, and the organisms often assumed bizarre forms. In some cases, however, the pneumococci again returned to the sputum after two to four days. Our own scattered observations in sulfapyridine treated cases indicate that the decline in the number of organisms, as already noted, is usually more rapid and more marked and persists during adequate therapy provided the pneumococcus is a susceptible one.

Frisch also found that following the administration of type specific antipneumococcus horse or rabbit serum, clumping of the extracellular pneumococci occurred, and in some cases a definite or marked increase in phagocytosis was noted. When such phagocytosis or clumping occurred in untreated cases it was interpreted as representing the development of immunity. The findings in the serum-treated cases are of interest in view of the conflicting evidence concerning the penetration of specific antibodies into the pneumonic lung. They suggest that the antibody may penetrate the infected lung at least at the periphery of the lesion from which the sputum is presumably coming.

Wood's<sup>124</sup> recent studies of experimental pneumonia in rats indicate that penetration may occur even into the center of the consolidated lung. He found clumping *Quellung* and phagocytosis in his experimentally produced pneumonic rat lungs following the administration of type specific rabbit serum.

### *Immunity after Sulfapyridine Treatment*

Type specific antibodies develop in sulfapyridine treated pneumonia patients at about the same time in the disease as in similar patients who recover spontaneously.<sup>122-126</sup> The same findings have been noted in treated animals recovering from experimental pneumococcal infections.<sup>128, 129, 130</sup> The time when such antibodies appear is independent of the "crisis" when thus induced by sulfapyridine treatment, and their appearance is often delayed for a week or even longer after the temperature has reached normal. Kneeland's<sup>2</sup> findings of a low rate of antibody production in drug-treated cases may be explained by his choice of the precipitin reaction as a test for antibody formation. This test, in our experience, is too crude to detect the low titers of antibody developed by most pneumonia patients. Our own<sup>127</sup> studies indicated that there is probably no difference between spontaneously recovered cases and those recovering following drug therapy, both as to the frequency with which antibodies develop and as to the titers attained.

The late occurrence of antibodies is the usual explanation offered for the relapses so frequently encountered in drug-treated cases, particularly when the treatment is discontinued too soon. Tests for antibodies, either by the Francis<sup>131</sup> skin test with type-specific carbohydrate<sup>126</sup> or by the Sabin<sup>13</sup> stained slide agglutination test of the serum with homologous type pneumococci<sup>123</sup> have been suggested as possible guides for discontinuing drug therapy. While useful in certain doubtful cases, these tests are hardly to be recommended for general use in drug-treated cases, since, in the great majority of patients, the treatment may be stopped safely before these tests become positive. On the other hand, when specific serum is used, either alone or in conjunction with chemotherapy the Francis test may be a useful guide to dosage.<sup>131, 132, 133</sup> When so used, it is essential to carry out a control test with the same material before any serum is given. The positive skin test after serum may be used as evidence for adequate dosage only when the control test gives no reaction.

### *Drug Resistance or Fastness*

Pneumococci have been shown to vary in their

susceptibility to the action of the same sulfonamide drugs both in vitro and in therapeutic experiments in animals<sup>135-141</sup> The differences in susceptibility are a characteristic of the individual strains and bear no relation to the type, although drug resistance of various degrees may be more frequent among the strains of certain types than it is in other types<sup>93</sup> Resistance to sulfapyridine may be induced in previously susceptible strains both in vitro<sup>142</sup> and in animals with experimental infections that have been treated with subeffective amounts of drugs<sup>136 143 144</sup> Ross<sup>145</sup> has reported a case of pneumococcal meningitis in which resistance was apparently acquired in the course of two or three days of treatment with sulfapyridine

In recent studies we<sup>93</sup> have succeeded in taking pneumococcus strains which were initially susceptible to the bacteriostatic action of sulfapyridine, sulfathiazole and sulfamethylthiazole and in making them resistant by growth in media containing increasing concentrations of these drugs Strains accommodated in this manner to growth in one of the drugs not only acquired a high degree of resistance against the homologous drug, but also became resistant to the other two chemicals to approximately the same extent Individual strains were found to vary in the ease with which fastness could be acquired in this manner Strains of pneumococci isolated from patients with pneumonia or with purulent infections before treatment with drugs was started were almost all highly susceptible to sulfapyridine, sulfathiazole and sulfamethylthiazole in vitro in concentrations readily attainable in ordinary therapy We found great differences among individual strains and types The greatest resistance was found among certain strains of the recently classified Type 33<sup>146 147</sup> On primary isolation, some of them grew freely in concentrations as high as 60 mg per 100 cc of each of the three drugs studied

We have also studied strains of pneumococci isolated from patients after several days of drug therapy and during a relapse of the pulmonary infection, and found them relatively resistant to the three drugs In 2 such cases pneumococci of the same type isolated before the beginning of drug therapy were highly susceptible The strains from these patients were equally resistant to sulfapyridine, the drug used in the treatment, and to sulfathiazole and sulfamethylthiazole Our find-count for certain failures of chemotherapy They also indicate that resistance may be acquired in the course of therapy and may thus account for relapses of the infection while treatment with the drug is being maintained As a result it is probably futile to

change from sulfapyridine to sulfathiazole, or vice versa, in cases in which relapse occurs during apparently adequate therapy with one of these drugs or when adequate therapy is not successful in terminating the disease Fortunately, the acquisition of drug-fastness in no wise alters the type specificity of pneumococci or their susceptibility to the action of homologous immune serum Type-specific serum should be used in such cases, and was used successfully in 2 of our cases These findings offer another argument for continuing the practice of typing in patients with pneumonia before beginning chemotherapy

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CASE RECORDS OF THE  
MASSACHUSETTS GENERAL HOSPITALANTE-MORTEM AND POST-MORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., Editor

## CASE 26391

## PRESENTATION OF CASE

A fifty-two year-old Italian steel chipper was admitted to the hospital complaining of pain in the right chest

The patient was well until about six and a half months before admission when he developed a severe toothache with pain and swelling in and around his mouth and face. The distress became so severe that he was forced to stop his work as a "steel chipper" in a large manufacturing concern which he had performed for twenty-two years. It was alleged that steel and sand dust were constantly in the air that at least 50 companion employees had died of consumption while he had worked there but that none of these had died during the five year interval before the patient's admission. Because of severe pain in the jaw and mouth the patient was able to take nothing but liquid nourishment. Six days later he consulted a dentist and a physician and was treated with cold packs to the face for some three weeks without much change in his condition. X-ray studies at this time failed to show any evidence of pus. He was treated symptomatically for a short time and was finally referred to a "specialist," who immediately pulled two lower front teeth and incised the right lower gum. No pus was found but the pain was relieved, and the swelling decreased slightly. Two days later, while climbing stairs, he suddenly felt a sharp pain in his right chest, and noted a rubbing sensation and "could hear something going pooh-pooh" during respiration. He fainted, was soon revived, climbed another flight of stairs, and then fainted again. A local physician was called who referred the patient to an outside hospital where four days later his chest was tapped and 7 ounces of fluid removed. A pleural effusion which he had had for some six or more days was now normal, and he felt better for four to five days. His temperature then rose again and he expectorated 6 to 8 ounces of foul-smelling sputum daily. He remained in the hospital for months without relief although the chest was tapped again. Furthermore he had "lumps" in the neck and axillae, and "lumps" in the chest wall.

still complaining of transient chest pain which was relieved by wearing a binder around the chest. He continued fairly well for about three weeks, coughed up bloody sputum only twice and was comparatively free of pain. He began to walk about the house and to sun himself on the roof, and was raising only 3 ounces of sputum daily. While at home, however, he developed a painful grapefruit sized lump in the right upper back. He ran a daily elevation of temperature, felt weak and anorexic, and lost weight. These symptoms continued he failed to improve, and finally he was admitted to this hospital.

The family marital and past histories were non-contributory.

Physical examination revealed a well-developed and well-nourished pale, perspiring man who looked feverish and chronically ill. He coughed frequently, raised purulent sputum with flecks of blood and complained of chest pain. The eyes showed a slight retinal arteriosclerosis, with bilateral arcus senilis. The teeth were carious, two were absent and there was pyorrhea, but no other oral abnormalities were noted. The neck presented two pale submental scars. The excursions of the chest were greatly diminished on the right, and there was a definite, non-fluctuant, markedly tender bulge over the right lower chest posteriorly, below the angle of the scapula. This area was flat to percussion but was neither red nor hot, there were diminished to absent tactile fremitus, breath sounds and whispered and spoken voice over it, but a few fine inspiratory rales were audible. Bronchial breathing was heard in the right axilla where there was dullness to percussion. There were fine inspiratory rales at the left base with loud consonating rales in the left axilla, without dullness. The left border of the heart was percussed at a point 10 cm beyond the midline in the fifth interspace. The heart rate was 120, the rhythm was regular and a moderately loud systolic murmur was heard at the apex. The blood pressure was 120 systolic, 80 diastolic. The abdomen was obese. The remainder of the examination was negative.

Examination of the blood showed a red-cell count of 5,080,000 with 60 per cent hemoglobin and a white-cell count of 17,800 with 87 per cent polymorphonuclears. The smear showed moderate variation in size and shape of the red cells, with anisocytosis and poikilocytosis. The sputum was thick, mucopurulent but otherwise negative. Stools were soft formed brown and guaiac negative. A tuberculin test using a 1:500,000 dilution was negative. Blood sugar and blood protein determinations were normal.

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CASE RECORDS OF THE  
MASSACHUSETTS GENERAL HOSPITALANTEMORTEM AND POSTMORTEM RECORDS AS USED  
IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

## CASE 26391

## PRESENTATION OF CASE

A fifty-two-year-old Italian steel chipper was admitted to the hospital complaining of pain in the right chest.

The patient was well until about six and a half months before admission when he developed a severe toothache, with pain and swelling in and around his mouth and face. The distress became so severe that he was forced to stop his work as a "steel chipper" in a large manufacturing concern which he had performed for twenty-two years. It was alleged that steel and sand dust were constantly in the air that at least 50 companion employees had died of consumption while he had worked there, but that none of these had died during the five year interval before the patient's admission. Because of severe pain in the jaw and mouth the patient was able to take nothing but liquid nourishment. Six days later he consulted a dentist and a physician and was treated with cold packs to the face for some three weeks with out much change in his condition. X-ray studies at this time failed to show any evidence of "pus." He was treated symptomatically for a short time and was finally referred to a "specialist" who immediately pulled two lower front teeth and incised the right lower gum. No pus was found, but the pain was relieved, and the swelling decreased slightly. Two days later while climbing stairs, he suddenly felt a sharp pain in his right chest and noted a rubbing sensation and "could bear some thing going pooh pooh" during respiration. He fainted was soon revived climbed another flight of stairs, and then fainted again. A local physician was called who referred the patient to an outside hospital where four days later his chest was tapped and 7 ounces of fluid removed. A fever which he had had for some six or more days fell to normal and he felt better for four to five days. His temperature then rose again and he began to expectorate 6 to 8 ounces of foul smelling bloody sputum daily. He remained in the hospital for three months without relief although the amount of sputum diminished. Furthermore he developed bilateral slightly tender swellings in the submandibular regions, which were successfully drained. One and a half months before admission he was discharged from the outside hospital,

still complaining of transient chest pain which was relieved by wearing a binder around the chest. He continued fairly well for about three weeks, coughed up bloody sputum only twice and was comparatively free of pain. He began to walk about the house and to sun himself on the roof, and was using only 3 ounces of sputum daily. While at home however, he developed a painful grapefruit sized lump in the right upper back. He ran a daily elevation of temperature, felt weak and anorexic, and lost weight. These symptoms continued he failed to improve, and finally he was admitted to this hospital.

The family, marital and past histories were non-contributory.

Physical examination revealed a well-developed and well-nourished pale, perspiring man who looked feverish and chronically ill. He coughed frequently raised purulent sputum with flecks of blood and complained of chest pain. The eyes showed a slight retinal arteriosclerosis, with bilateral arcus senilis. The teeth were carious, two were absent and there was pyorrhea but no other oral abnormalities were noted. The neck presented two pale submental scars. The excursions of the chest were greatly diminished on the right, and there was a definite, non-fluctuant, markedly tender bulge over the right lower chest posteriorly, below the angle of the scapula. This area was flat to percussion but was neither red nor hot, there were diminished to absent tactile fremitus, breath sounds and whispered and spoken voice over it, but a few fine inspiratory rales were audible. Bronchial breathing was heard in the right axilla where there was dullness to percussion. There were fine inspiratory rales at the left base with loud consonating rales in the left axilla without dullness. The left border of the heart was percussed at a point 10 cm. beyond the midline in the fifth interspace. The heart rate was 120 the rhythm was regular and a moderately loud systolic murmur was heard at the apex. The blood pressure was 120 systolic, 80 diastolic. The abdomen was obese. The remainder of the examination was negative.

Examination of the blood showed a red-cell count of 5,080,000 with 60 per cent hemoglobin and a white-cell count of 17,800 with 87 per cent polymorphonuclears. The smear showed moderate variation in size and shape of the red cells with achromia. The sputum was thick mucopurulent but otherwise negative. Stools were soft formed brown and guaiac negative. A tuberculin test using a 1:500,000 dilution was negative. Blood sugar and blood protein determinations were normal.

Roeniggenograms of the chest and fluoroscopy

revealed that the diaphragm was normal in position, but that the right had markedly impaired motion. The greater part of the right lower lobe in its posterior portion showed consolidation, and there was a cavity in its upper portion that contained air and fluid. The left lung field showed an increase in the linear lung markings, with some mottling. Another film, which included the posterior chest wall, showed the presence of a large cavity along the posterior chest wall on the right side containing air and fluid and extending from the sixth dorsal vertebra downward to the diaphragm.

The temperature was 102°F, the pulse 120, and the respirations 25.

About three days after admission the mass over the right posterior chest became fluctuant, and extended from the level of the eighth rib to that of the second lumbar vertebra. The patient seemed to be fairly comfortable while resting on the left side. He was given supportive care, a transfusion and adequate sedation, and on the ninth hospital day, incisions and drainages of the fluctuant mass, the empyema and the lung abscess were performed under local anesthesia. There was moderate drainage of foul-smelling purulent material, and the temperature fell slightly, but continued to spike daily from 99 to 101°F. A culture of this material showed no growth aerobically, *Staphylococcus aureus* grew anaerobically. Dressings of the wounds were performed periodically, sometimes under Evipal anesthesia. X-ray films of the chest showed no fluid and some decrease in the size of the cavity. About three weeks after the initial operation several small "furuncles" appeared—two in the skin of the neck, one in the skin of the left upper quadrant of the abdomen, and another in the sole of the right foot. The latter two soon "pointed," and were incised and drained. It was noted that in these lesions, as in the chest wound, the non-odorous pus had burrowed deeply in the fascial planes surrounding each of them. Cultures of the pus from the abscesses revealed an anaerobic *Staphylococcus aureus*. The patient was placed on a sulfapyridine regime and the blood level rose to 7.4 mg per 100 cc. The temperature fell slightly, and he improved somewhat. The neck lesion then became fluctuant, and was incised and drained. Among other things he was given multiple transfusions. He slowly improved; the temperature fell gradually to normal, and he seemed to be symptomatically well, although the lesions were not completely cured since there was still drainage of purulent material from the chest wound and many of the skin lesions. He was finally discharged to a chronic-disease hospital on the sixty-second hospital day.

## DIFFERENTIAL DIAGNOSIS

DR. AUBREY O HAMPTON This is the area described at the region of the apex of the lower lobe. It is a large cavity and contains fluid. It has a rather thin, sharply defined wall, not the thick indurated wall you sometimes see.

DR. FREDERICK T. LORD How about the mottling in the rest of the lung fields? The man had been exposed to silica. What about the question of tuberculosis?

DR. HAMPTON There are changes through the mid-portion of the left lung field that might be due to silicosis, but I should question very much if a diagnosis of tuberculosis was made. The cavity has a thin wall, and it might be tuberculous.

DR. LORD You shake my faith.

DR. HAMPTON I do not know the answer. I might mislead you.

It is interesting that you can see the diaphragm through this dull area; the lesion is more in the lung than in the pleura, although in the lateral view it extends quite far posteriorly.

DR. LORD We know he had something in the pleura—unless they tapped the abscess cavity.

DR. HAMPTON The abscess is very close to the chest wall, and they could have tapped it.

DR. LORD Perhaps they did tap the abscess.

Three days after admission the mass over the right posterior chest became fluctuant. We do not see it, do we?

DR. HAMPTON I think it is up in here.

DR. LORD It extended from the eighth rib to the second lumbar vertebra. It is said to have been due to an empyema.

We have a patient of fifty-two who worked with dust for a long time. He had an initial disturbance about the jaws, and within a month there was a rather sudden onset of pulmonary disturbance. One of course would think of an infected embolus which had given rise to lung abscess and empyema, which we know he had. One would like to know whether or not the original fluid was bloody. The pulmonary process is very likely secondary to the jaw disturbance. I cannot settle the question of embolism, and I presume no one could. After a couple of months he again had a disturbance about the jaw, and then, three weeks before entrance, he developed an abscess over the right back, with signs that are not of any special interest because we know the findings from the surgical record. He had a secondary anemia with leukocytosis. We do not know the results of blood culture.

DR. TRACY B. MALLORY A blood culture was taken, one flask showed diphtheroids, and the other, no growth.

DR. LORD The diphtheroids were probably due to contamination

DR. MALLORY I should think so

DR. LORD A tuberculin test with 1:50,000 dilution was negative. I should say that the chances were that this man had had tuberculosis. He had been exposed to the disease in his work. It is said that there had been 50 deaths from tuberculosis among those who worked with him, and yet the tuberculin test was negative. I do not believe any importance should be attached to it. Old tuberculin is variable in strength and difficult to standardize. Was old tuberculin used here?

DR. MALLORY Yes

DR. LORD Furthermore, it is undesirable to rely entirely on such a highly dilute solution of tuberculin. The most satisfactory method is an intracutaneous test with 0.1 cc. of a 1:10,000 dilution and if this is negative, a second test with 0.1 cc. of a 1:1000 dilution. If this is also negative, the patient should be tested and fail to react to 0.1 cc. of a 1:100 solution before tuberculosis can be excluded.

With the history of an initial disturbance about the jaw followed by a pulmonary process, infection with *Actinomyces bovis* must be considered. Perforation of the chest wall, which occurs in over 80 per cent of the cases of actinomycosis, is still further suggestive of the ray fungus as the inciting agent. The streptothrix group of organisms may cause pulmonary lesions, and empyema and perforation of the chest wall may occur, but lesions about the head and neck are not to be expected.

To establish the presence of infection with *A. bovis* it is often necessary to look with particular care for the granules containing the parasite. The purulent exudate should be spread in a thin layer in a Petri dish and examined against a dark background. Suspicious particles should be removed, crushed between a slide and cover glass and examined under the microscope. Granules made up of a compact mass of branching gram staining filaments with radiating club-bearing filaments at the periphery may be regarded as actinomycotic granules. *A. bovis* is essentially an anaerobe and difficult to isolate in pure culture from material contaminated with bacteria.

The clinical aspects of this case are suggestive of actinomycosis, but not typical. Though a large accumulation of pus in an abscess, such as was present in this case, may occur with actinomycosis, it is uncommon. The lesions are usually indurated and made up of granulation tissue or containing multiple small abscesses.

I should like to ask if *A. bovis* was searched for particularly

DR. RALPH ADAMS Not in the beginning. The report was negative.

DR. LORD That is confusing, and we have to consider three possibilities. The first is tuberculosis, since a negative test with a 1:50,000 dilution of tuberculin cannot be relied on to exclude it. The x-ray findings, however, do not suggest tuberculosis. Furthermore, there was a leukocytosis, which is not likely to be present unless there is a mixed infection. On the whole, I am inclined to exclude tuberculosis. That leaves actinomycosis and a non-tuberculous suppurative process due to infection with a staphylococcus. Between these two, I may say that the clinical aspects were very suggestive of actinomycosis because of the jaw lesions and the perforation of the chest wall. Although empyema and a large accumulation of pus may occur with this disease, they are uncommon. The clinical course is unusually favorable for pulmonary actinomycosis, which has proved to be one of the most serious diseases with which we are confronted—there are only few reported recoveries. It is possible that sulfapyridine favorably modified the course, but we do not yet know what it will accomplish in the treatment of the disease and it should be carefully tried in a series of cases. Too few cases have thus far been treated with the drug to know the answer. If the lesion was a non-tuberculous suppurative process, sulfapyridine might have been helpful in treatment, but is more likely to be effective with septicemia due to this organism. There have been about a dozen cases of staphylococcal septicemia treated with sulfapyridine with apparent success.

I have to leave the diagnosis without reaching a decision between actinomycosis and staphylococcal infection, leaning a little more heavily toward the latter.

DR. DONALD KING We raised all these questions when we saw the patient on the ward. The other question was whether he had carcinoma of the bronchus with a secondary abscess, but that seemed unlikely.

DR. LORD Carcinoma has to be considered whenever there is a pulmonary abscess, but I believe these suppurative complications were on an infective rather than a carcinomatous basis.

#### CLINICAL DIAGNOSES

Empyema necessitatus  
Lung abscess

#### DR. LORD'S DIAGNOSIS

Staphylococcal pulmonary infection?  
Actinomycosis?

#### ANATOMICAL DIAGNOSIS

Actinomycosis

## PATHOLOGICAL DISCUSSION

DR. MALLORY Eventually from incision and drainage of one of the subcutaneous abscesses a fragment of tissue reached the laboratory and was looked at by several members of the staff, who noticed nothing but a marked chronic inflammatory process. Mr. John Homans, Jr., a third-year medical student, looked at the slide and said, "What is this?" And there was a well-formed actinomycotic granule. So I think we have the right to say that the fundamental process was actinomycosis. It is possible that there might have been a superimposed staphylococcal infection, inasmuch as staphylococci were grown on several occasions under anaerobic conditions. If so, it is possible that it modified the picture to some extent.

## CASE 26392

## PRESENTATION OF CASE

*First Admission* A fifty-one-year-old white, married native salesman entered the hospital complaining of asthma.

One month before entry he developed a mild head cold and two days later noted dyspnea and wheezing for the first time. Following this he had daily attacks of cough, dyspnea and wheezing on exertion and was orthopneic. He continued work until ten days after the onset of this condition. The family history revealed that a sister had hay fever and asthma and that a paternal grandmother had had asthma. Four years before entry all his teeth had been removed. The past history and family history were otherwise non-contributory.

Physical examination revealed a well-developed, moderately obese man who was somewhat dyspneic on exertion. The heart sounds were of poor quality but were regular. The aortic second sound was greater than the pulmonic. There were scattered moist rales posteriorly over both lung bases. The abdomen was tender in the right upper quadrant, but the liver edge was not palpable. There was slight pitting edema of the ankles. The blood pressure was 205 systolic, 140 diastolic.

The temperature was 98°F, the pulse 100, and the respirations 26.

The urine gave a + test for albumin and contained 2 red cells and occasional white cells per high-power field. The blood showed a red-cell count of 4,800,000 with 90 per cent hemoglobin, and a white-cell count of 10,500 with 71 per cent polymorphonuclears. The nonprotein nitrogen of the serum was 34 mg per 100 cc, the fasting blood sugar 95 mg, and the fasting cholesterol 215 mg. A blood Hinton test was negative. An

electrocardiogram showed slight left-axis deviation, late inversion of T<sub>1</sub> and an upright T<sub>4</sub>.

X-ray films showed the heart enlarged in all diameters, especially in the region of the left ventricle. No calcification was seen in the region of the aortic or mitral valve. Density was increased in the upper lobes of the lungs, the diaphragm was low. The general appearance was that of cardiac hypertrophy and dilatation, passive congestion in the lungs, fibrosis in the upper lobes and emphysema of the lower lobes.

Three days after entry he saw some visitors, and became very excited and tired. Following this he had a feeling of tightness in the chest and had difficulty in sleeping. The next morning it was noticed that the neck veins were slightly engorged. There was a split, apical first sound. The breath sounds were very distant, and a few moist rales were noted in the low bases after cough. There was no wheeze. The vital capacity was 1930 cc. On the sixth hospital night, dyspnea was severe and he slept little. He coughed considerably and complained of precordial oppression, not sudden in onset but severe and radiating to the left shoulder and scapular region. He showed faint cyanosis, had marked orthopnea and coughing and was in acute distress. The blood pressure was 170 systolic, 100 diastolic. The chest was full of moist rales that obscured the heart sounds. Digitalization was begun on that day. The following morning he complained of pain in the region of the cardiac apex and in the lower left chest posteriorly. He also had pain in the region of the right nipple. The temperature was 101°F, the pulse 100, and the respirations 28, the sputum was white. No rub was heard. The following day he stated that the sputum was blood tinged. On the twelfth hospital day the left base was very dull to percussion and breath sounds were absent. An x-ray film of the chest showed hazy dullness at the left base obscuring the outline of the diaphragm. In the lateral view most of the dullness was seen to lie anteriorly, rising along the anterior chest wall. There was thickening of the septum between the right upper and middle lobes, and the lower lobe was reduced in size. A chest tap at the left base yielded 400 cc. of light-yellow fluid. It had a cell count of 9000 with 63 per cent red cells, 31 per cent lymphocytes, 2 per cent polymorphonuclears and 4 per cent mononuclear cells. His condition gradually improved, and he was discharged on the seventeenth day.

*Final Admission* (eighteen months later) After discharge he remained in bed for five weeks, and two months later was able to return to work. He continued to work until about three weeks before re-entry, although the dyspnea gradually increased.

and he occasionally was somewhat cyanotic. He took digitalis intermittently. The blood pressure was 186 systolic, 126 diastolic, seven months before re-entry, and 220 systolic, 140 diastolic, three weeks before. During the three weeks before re-entry he became considerably more dyspneic and wheezed a good deal. He had difficulty in sleeping and had a persistent cough, productive of thick, yellow sputum without blood. He found it necessary to sleep on two pillows at night, and the ankles became very swollen.

Physical examination revealed an overactive, alert, slightly obese man showing Cheyne-Stokes respiration. There was exophthalmos and lid lag bilaterally. Examination of the fundi showed two small hemorrhages on the left and arteriovenous nicking bilaterally. The neck veins were engorged two thirds of the way to the angle of the jaw with the patient resting at a 45° angle. The heart was enlarged both to the right and left the dullness extending 4.5 cm to the right and 11.5 cm to the left of the midsternum. The sounds were rapid and of poor quality with gallop rhythm over the precordium. The aortic and pulmonary second sounds were equal. There was a soft systolic murmur at the apex. There was slight dullness with decreased breath sounds and voice sounds and moist rales over the left base posteriorly and low in the right axilla. A loud wheeze was heard in the left chest anteriorly. The blood pressure was 175 systolic, 110 diastolic. The liver was felt 3 cm below the costal margin. It had a tender smooth edge. No abdominal fluid could be demonstrated. Both lower extremities showed pitting edema extending to the knees.

Urine examination showed a specific gravity of 1.022, with a +++ test for albumin and 10 red cells and an occasional white cell per high power field. The red-cell count was 4,500,000 with 85 per cent hemoglobin and the white-cell count 10,400 with 76 per cent polymorphonuclears. The serum nonprotein nitrogen was 32 mg per 100 cc., and the protein 7 gm.

An electrocardiogram showed slight to moderate left axis deviation, a finding that suggested left ventricular strain, and an auricular rate of 150. X-ray films showed the heart extending almost to the left axillary line. There was dullness suggesting fluid at the left lung base, and diminished radiance throughout both lungs with thickening of the lung markings.

On the second hospital day the patient developed a sharp knife-like pain in the right side. It came on suddenly and was exaggerated with deep inspirations. It increased in severity and the patient became very pale, the skin moist and cold and the pulse rapid. The blood pressure was 160

systolic, 90 diastolic. The heart sounds did not change, but there was a friction rub in the right axilla. Morphine gave partial relief. The patient was very apprehensive about the condition, but the following day he was much better. During the night he had marked diuresis. Although the pain had gone a friction rub was still heard in the right axilla. Moist rales were sparsely scattered throughout the chest. The breath sounds were diminished in certain areas, loud in others. On the sixth hospital day the condition was essentially the same. The temperature had remained constant at 97 to 98.6°F., the respirations at 25 to 30. On the seventh hospital day an electrocardiogram showed a severe degree of heart block with a PR interval of 0.25 second and occasional dropped beats. A wide P wave, a slurring of the QRS complex and an absent R<sub>s</sub> suggested a change. T<sub>1</sub> and T were low, and ST<sub>s</sub> was elevated. There was a gallop rhythm and an auricular rate of 100. The pulse rate was increased, and the patient complained of abdominal distress and gas.

A sixth of a grain of morphine, a dose of Salix-gan and an enema were given on the seventh day. The following day the heart sounds were regular and the chest was clear except for fine moist rales at the left base. The patient was greatly improved and said he had spent the best night in years. On the eleventh hospital day he was again apprehensive, and dyspneic on exertion and the heart showed split first and second sounds. On the thirteenth day the dyspnea was worse and he had a Cheyne-Stokes type of respiration with cyanosis. Bronchial breathing was heard over the right upper lobe posteriorly. Only a few crackling rales were heard at the bases. The blood pressure was 230 systolic, 120 diastolic. The next day he was again remarkably improved. It was noted that the neck veins collapsed on inspiration. He had some expiratory difficulty and the diaphragm was low in position. During the night in spite of increased morphine, he was restless and on one occasion got out of bed. The cyanosis and Cheyne-Stokes respiration were relieved by the use of an oxygen tent. The heart was regular, and there were no remarkable chest signs to explain these symptoms.

On the fifteenth day the blood pressure dropped to 160 systolic, 100 diastolic but the heart sounds were regular and the pulse was 80. There were wheezing rales, and expiration was longer than inspiration. He was acutely disturbed mentally, delirious and overactive. The following day the blood nonprotein nitrogen was 44 mg. per 100 cc. The white-cell count was 12,000 with 85 per cent polymorphonuclears. Harsh breath sounds were

heard under the right clavicle, with coarse rales. The left base was relatively dull to percussion. He had no peripheral edema or ascites. The blood pressure was 180 systolic, 120 diastolic. On the twentieth hospital day he was essentially the same but looked somewhat better and, although drowsy, talked rationally. There was gallop rhythm along the right border of the sternum, and a sinus arrhythmia was noted.

He died quietly on the twenty-second hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR. PAUL D. WHITE. Asthma is most commonly the result of a reaction to disease of the lung or pleura of an anaphylactic reaction, or of a reflex due to pulmonary congestion from heart disease. Several causes may act simultaneously.

This patient's family history is not important. Most families will show at least one member with asthma or hay fever.

"The heart sounds were of poor quality." That is important if the poor quality was not the result of pulmonary emphysema. "The aortic second sound was greater than the pulmonic." It would be of some importance to know if either one was accentuated. I should judge that they must have been accentuated, at least the aortic. The rales could have resulted from respiratory infection as well as from congestive heart failure. The edema of the ankles is not very important. It may be due to local circulatory trouble or obesity—he was a heavy man. The liver was not enlarged. Slight pitting edema of the legs may come, however, before the liver grows very large.

Then we arrive at the first important point so far as the circulation is concerned—the blood pressure. It indicates that the heart may have played a role in this asthma and dyspnea, but there is no statement as yet of heart size and evidently there were no heart murmurs.

The laboratory tests were all relatively normal,—the cholesterol was on the upper edge of normal,—helping to rule out the later suggestion of thyrotoxicosis.

I have looked at the electrocardiogram and found that there is only slight inversion of T<sub>1</sub>, not very impressive, but nevertheless abnormal. An upright T<sub>4</sub>, if the record was taken according to the old technic, is evidence of disease. The left-axis deviation is significant. The changes do suggest coronary disease, aside from left ventricular enlargement.

"X-ray films showed the heart enlarged in all diameters." That is the second important point. May we see the first x-ray film?

DR. AUBREY O. HAMPTON. It does appear that the upper lobes are dense, particularly on the left

side in the region of the upper lobe, and the lungs fairly radiant at both bases in spite of the fact that there is beginning pleurisy or pleural effusion on the left side. The blood vessels are large on both sides and are visible even to the periphery of the lungs. The heart shadow is a little wider across the base than is usual with simple left ventricular hypertrophy. This may be due to decompensation.

DR. WHITE. I should be in favor of cardiac enlargement from hypertensive heart disease, with some cardiac failure and some change in the lungs.

"he had a feeling of tightness in the chest." The question comes up as to the significance of this feeling of tightness. It was possibly due to coronary thrombosis. That is the third important point in this story of heart failure. There was evidence of right-sided heart failure, hence confirming the suspicion that the left heart had already failed.

The respiratory infection may have had more to do with the earlier dyspnea than had the heart failure, although there may have been subsidence of congestion of the lungs when right-sided heart failure began.

The pain in the region of the cardiac apex and left chest suggests pulmonary infarction rather than coronary thrombosis. The temperature, pulse and sputum would fit in with pulmonary infection. May we see the x-ray films taken at that time?

DR. HAMPTON. This film was taken eleven days after the first. It seems to show a smaller heart and an accumulation of fluid at the left base. Also both lung roots look smaller at the time when he was apparently getting worse. There is this queer shadow posteriorly, which apparently is on the left side in the costophrenic angle. It is convex upward instead of the usual concavity of fluid, which he previously showed in the costophrenic angle. We have seen this picture with infarcts, particularly those in the costophrenic angle.

DR. WHITE. He had been taking digitalis, and this fact may have had a great deal to do with his improvement. His doctors should have begun it earlier, of course, probably at admission when he complained of dyspnea. I think it would be quite interesting to know whether he was already under the influence of digitalis and had benefited from that before the second film was taken. The decrease in heart size may have been the result.

"During the three weeks before re-entry he became considerably more dyspneic and wheezed a good deal." We do not know that there was respiratory infection at that time, but the sputum suggests it. We do not get thick, yellow sputum from pulmonary infarction alone or from congestive failure. It is conceivable that he had a per

or recurrent pulmonary infection. I do not see we have any clear evidence that he had uretasis, but he may have had it could like to ask if the sputum was examined for bacilli. Why should he have had so much sputum unless he had some infection?

TRACY B. MALLORY The sputum was negative for tubercle bacilli.

WHITE "There was exophthalmos and lid edema laterally. That is the only suggestion of toxemia and there is nothing else to bear on it.

I think we can ignore it. A loud wheeze was heard in the left chest only. As a rule with congestive failure the rales are more definite on the right side rather than on the left. This finding suggests that he is remains of an infarct or infection in the

pitting edema extending to the knees means congestive failure approaching the end.

HAMPTON In this film the heart has increased markedly in size and the pulmonary vessels markedly dilated. The density at the left is not so marked as that at the examination two years before, but there is definite evidence of pleural disease.

WHITE A significant point is that the pulse rate was so rapid. Whether that was due to a new rhythm plus heart block resulting from the heart disease and failure I do not know. The rate is distinctly more rapid—150 as compared to 100 a few days before. I judge he had been continuing with digitalis. Sometimes overdigitalization will produce a disturbance of this kind but we have no proof of that here, the T waves do not seem to indicate poisoning from digitalis.

summary I shall put down that he had hypertension and probably also coronary heart disease as shown better by the electrocardiogram than by the clinical signs, with congestive heart failure precipitated by acute pulmonary infection or infarction and complicated by multiple myocardial infarcts. Pulmonary infection is indicated by the thick yellow sputum. Cancer of the lung is a remote possibility.

#### CLINICAL DIAGNOSES

Essential hypertension  
Generalized arteriosclerosis  
Nephrosclerotic and hypertensive heart disease  
Cardiac decompensation  
Coronary occlusion  
Bronchopneumonia

#### DR. WHITE'S DIAGNOSES

Hypertensive and coronary heart disease.  
Congestive heart failure.  
Pulmonary infarction or infection  
Multiple myocardial infarcts

#### ANATOMICAL DIAGNOSES

Hypertrophy of the heart, hypertensive type  
Myocardial fibrosis  
Coronary sclerosis with thrombosis.  
Bronchiectasis, right upper lobe.  
Pulmonary infarction healed, left lower lobe.  
Bronchopneumonia  
Nephrosclerosis  
Arteriosclerosis, cerebral  
Chronic passive congestion

#### PATHOLOGICAL DISCUSSION

DR. MALLORY As Dr. White predicted, the most important underlying process in this patient was hypertensive heart disease. The kidneys showed extensive vascular disease of the type regularly associated with chronic benign hypertension. The heart itself weighed 800 gm., with hypertrophy and dilatation of all the chambers but with preponderant changes on the left side. The left coronary artery was markedly sclerotic, and a fresh thrombus was found in the left descending branch. No corresponding area of acute infarction could be made out in the myocardium but the left ventricle showed extensive patchy fibrosis and rather marked thinning of its walls at the apex.

From the pathological point of view the most interesting findings were centered in the lungs. The density noted on x-ray examination in the right upper lobe field was due to a fairly extensive area of bronchiectasis which extended up from the middle lobe septum in a triangular area 6 cm. in length and 4 cm. in width at its lower margin. In the left lower lobe at the costophrenic angle was an area of marked thickening of the pleura with underlying fibrosis of the pulmonary parenchyma about 1 cm. in width. On microscopic examination this showed complete obliteration of the lung architecture with dense masses of intertangling elastic fibrils, a characteristic appearance of a healed infarct of the lungs. Several vessels in the immediate neighborhood showed recanalized thrombi. This clearly checks with the episode of his first admission when he had sharp pleural pain in the lower left chest, dullness at the left base on x-ray examination and hemoptysis. The other findings of significance were a slight terminal bronchopneumonia and rather extensive cerebral arteriosclerosis with many minute microscopic areas of softening of the brain.



test Modern football demands of the player a splendid discipline, self-control and a subordination of the individual to the team Today it might well be given a place in the list of those character-building activities William James suggested in his essay, "The Moral Equivalent of War"\* Whether these good qualities outweigh the evils of "overemphasis" and "a game for gate receipts only" is debatable Without taking sides on this point, it cannot be denied that there are few universities, colleges or even schools which have not been accused of professionalism in football to a greater or less degree

The element of serious injury to the player is far less of a problem today than it has been in the past However, as is pointed out in an article in this issue of the *Journal*, safety for the player is apparently to be obtained only with careful supervision by a competent personnel The author quotes figures that seem to show that the danger of serious injury in this sport is at a minimum only when there is adequate medical supervision and when the rules are enforced by competent officials He very properly states that it is in the unsupervised games that serious injury is most likely to occur, and also suggests that his figures show that serious injuries can be prevented under nearly ideal conditions Such conditions, however, are not obtained in a large percentage of cases As long as the colleges play football the schools will probably do likewise, as will the groups of sand-lot players

There is one aspect of this question that is seldom referred to, although it has an important bearing on the large number of seriously crippling joint injuries Thirteen to seventeen years cover the ages of most schoolboy and "sand-lot" participants of this game For many boys this is a period of rapid skeletal growth, and their muscular and ligamentous strength does not always keep pace with their bony growth "Their legs are long and their joints are loose," they are clumsy, and they do not co-ordinate well To

subject them to the danger of joint injury during an age when their joints lack the normal muscular and ligamentous support that will come a year or two later is to court disaster Knee injuries at this age may, and often do, result in a joint that is never again able to stand the stress of even ordinary sports It is probable that a number of boys incapacitated for college football because of knee injuries sustained in secondary schools is far larger than is shown by any available statistical data And it is not only at the schools with inadequate medical supervision that such accidents occur

No trainer of race horses would allow a two-year-old to run in steeplechases To do so would almost inevitably result in a "breaking down" of the joints, he is then of no further use in racing and is often "destroyed" In many cases, the boy of thirteen to seventeen is similar, structurally and physiologically, to the two-year-old colt And, if so, his joints should not be subjected to the stresses of football The coach who appreciates the dangers inherent to this age group is a great rarity Even a greater rarity is the coach who will not allow a rapidly growing, though perhaps fast and heavy, boy to take part in the sport There have been times when it has seemed that the fate of the "broken-down" colt had better been meted out to the enthusiastic but woefully ignorant coach who allows a candidate of this age and type to play the game

The professional athlete appreciates that he is only as strong as his legs, and he spends many hours of drudgery on "road work" The average schoolboy concentrates on a beautifully developed torso and arms With walking now reduced to a minimum, a pair of sturdy legs and knees is far less common than it was in the days before the automobile

If schoolboy football is to be reasonably safe only when medical supervision of the elaborate and expensive type advocated in this article is furnished for all participants of all ages, one might well ask, Is it worth while? and, Is it a game?

\*James W. *Memories and Studies* 411 pp New York Longmans Green & Co 1911

## E. EPONYM

## DUPUYTREN'S CONTRACTURE

published description of this condition *Leçons orales de clinique chirurgicale tel-Dieu de Paris* by Guillaume Dupuy (1835), chief surgeon of the hospitalists of a series of lectures collected by students and published at Paris in 1832.

of the translation from Rétraction : des doigts par suite d'une affection vrose palmaire [Permanent Retraction Following an Affection of the Palmaris] follows

on investigation one might find descriptions and in the works of other authors but devoted as it is to action, has not permitted them all, and I shall be very happy to learn who have preceded me and have written a condition have found the cause and the means to be employed for its cure. Those who have a predisposition to the condition are describing notice that extension of the affected hand is less easy than before.

finger is soon drawn down. The changes perceived in the first finger and the others in proportion to the progress of the disease, finger is more and more contracted. It is at that flexion of the two neighboring fingers.

When the ring finger is markedly flexed, the skin shows folds with the concave side of the finger and the convex toward the articulation with the radius. These folds are of natural adhesions between the skin and the structures beneath. If one palpates in aspect of the ring finger a tense cord is

R W B

## MASSACHUSETTS MEDICAL SOCIETY

OF OBSTETRICS  
GYNECOLOGY\*

ALMOND S. TITUS, M.D., Secretary  
330 Dartmouth Street  
Boston

SECTION FOLLOWED  
PNEUMONIA

3, a thirty-eight year-old essential para the hospital in mild labor on September

ly history, was negative except that one tuberculosis. The patient's past history included the usual children's diseases. She had been more or less all her life. There was no history of tuberculosis, which had never

been proved. The appendix and an ovarian cyst had been removed in 1930. Catamenia began at fourteen, were regular with a twenty-eight-day cycle and lasted five days. The first pregnancy terminated in a miscarriage at two months and was followed by the above operation one month later. The second pregnancy ended in a difficult, high forceps delivery after a thirty hour labor. The present pregnancy had been normal in every respect.

As the head did not engage, a low-cervical cesarean section was done at 8 a.m. on September 20. There were no complications, and a female child weighing 6 pounds, 15 ounces, was delivered in good condition. A clots of 1000 cc. of 5 per cent glucose solution was given at the close of the operation, and the patient was returned to bed in good condition.

On September 21, the temperature was 101 to 103°F., the pulse 110 to 140, and the respirations 20 to 30. The patient coughed and raised mucus all night. A diagnosis of pneumonia was made, and sulfapyridine started 15 gr. every four hours. On September 22 the temperature was 101 to 102°F., the pulse 110 to 130 and the respirations 30. The patient was still coughing, and was nauseated.

On September 23 the patient became steadily worse. The temperature was 102.8°F., pulse 130, and the respirations 30. Sulfapyridine was discontinued, and Prontosil started, 5 cc. every four hours for three doses. The next day the temperature, pulse and respirations were still elevated and nausea and vomiting continued. The Prontosil was discontinued, and sulfapyridine started again at 6 p.m., 10 gr. every four hours with sodium bicarbonate. On September 25 the sulfapyridine was increased to 15 gr. every four hours. The patient's condition was little changed; the temperature was 101.5°F., the pulse 132, and the respirations 50.

The patient gradually grew worse and she was placed in an oxygen tent on September 26. Sulfapyridine was omitted at 6 p.m. on September 27. The following day the temperature was 98.6 to 100.5°F., the pulse 130 to 140 and the respirations 40 to 50. Her condition was very bad, and she was given two doses of insulin, 10 units at 4.35 a.m. and 20 units at 8.30 a.m. The patient was seen in consultation at 11.45 p.m. The consultant's note reads as follows: Evidence of pulmonary consolidation exists in both chests posteriorly, front and back; there are numerous rales, moderately moist but not marked. The heart is regular and rapid, and the sounds are of fairly good quality. The blood pressure is 130 systolic, 80 diastolic. The color is fair. The patient is restless, with rapid

\*Selected case histories by members of the section will be presented and questions by subscribers are solicited and answered by members of the section.



T—WALTER A. BARTLETT M.D., aged fifty  $\pi$  died on August 12 at the Glenclyffe Sanatorium an illness of several months. He was graduated from Dartmouth Medical 111 He served his internship at the Mary Hospital in Hanover and then pursued special New York City before starting the practice in Manchester in 1912. He had been a member of Education for eight years. Dr. A member of several social and fraternal or as well as local county and state medical

are his widow Mrs. Hazel M. Bartlett, three A., Jr., Arnold W. and Thomas E. Bartlett, iter

TH—CHESTER L. GOLDSMITH M.D., who l in Winchester New Hampshire, for seven- at the age of sixty years on July 26. nith graduated from the Maryland Medical lsumore in 1912. He also did undergraduate lton University in Baltimore and at Johns versity School of Medicine. nith was a member of the Odd Fellows and

I—FRANK J. PHERSON M.D., of Manches- iture, after a short illness, on August 27. He ditioned at the Boston Medical College in 1908 and 31 1940

re By Mount S. thorough nberg has been appointed profes- na. Philadel yrology at the School of Medi- Medicine City. He was formerly profes- By lagonomy at the University of Ber- Sigenstadt made visiting professor of cytology noprof 1919 at St. Louis, and in 1939 a mem- nute, Philadelphia.

Mental announced that Dr. Edwin B. Ast- erintendent at the Johns Hopkins Uni- il or Medicine, will become assistant profes- niotherapy at the Harvard Medical School er of the medical staff of the Peter Bent spital.

# EMENT

WEISS, M.D., announces the removal of his 371 Commonwealth Avenue to 483 Beacon

## PRATT DIAGNOSTIC

Bennet Street Boston  
Lecture Hall 9-10 a.m.

CONFERENCE PROGRAM OCTOBER-NOVEMBER  
tober 1—Differential Diagnosis of Certain of the Spine. Dr. J. D. Adams.  
October 2—Hospital case presentation. Dr. Thannhauser  
October 3—Cardiovascular Clinic. Dr. John  
ber 4—Carcinoma of the Breast. Dr. E. M.

Saturday October 5—Hospital case presentation. Dr. S. J. Thannhauser  
Tuesday October 8—A Case Study of Adrenal Deficiency in an Infant. Drs. F. C. McDonald and N. T. Werthesen.  
Wednesday October 9—Hospital case presentation. Dr. S. J. Thannhauser  
Thursday October 10—Immunity in Upper Respiratory Infections. Dr. Leonard Asher  
Friday October 11—Routine Office Cardiovascular Dis- ease. Dr. S. A. Levine.  
Saturday October 12—Hospital case presentation. Dr. S. J. Thannhauser  
Tuesday October 15—Steroid Hormone Excretion Rates Associated with Dysmenorrhea. Drs. N. T. Werthesen and R. E. Brownlee.  
Wednesday October 16—Hospital case presentation. Dr. S. J. Thannhauser  
Thursday October 17—Nephritic Clinic. Dr. R. W. Buck.  
Friday October 18—Recent Advances in Anesthesiology. Dr. F. W. Marvin.  
Saturday October 19—Hospital case presentation. Dr. S. J. Thannhauser  
Tuesday October 22—Title to be announced.  
Wednesday October 23—Hospital case presentation. Dr. S. J. Thannhauser  
Thursday October 24—Hemorrhagic Diathesis. Dr. Eugene Lozner  
Friday October 25—Clinicopathological conference. Dr. Fuller Albright.  
Saturday October 26—Hospital case presentation. Dr. S. J. Thannhauser  
Tuesday October 29—Food Allergy. Dr. E. A. Brown.  
Wednesday October 30—Hospital case presentation. Dr. S. J. Thannhauser  
Thursday October 31—Title to be announced.

## BOSTON DOCTORS SYMPHONY ORCHESTRA



The Boston Doctors Symphony Orchestra will resume rehearsals under Alexander Thiede, on Thursday evening, October 10. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham

Hall Hotel Brookline (BEA 2430)

## CHILDREN'S HOSPITAL

Beginning October 2 the weekly clinicopathological conferences at the Children's Hospital will be held every Wednesday at 12:00 noon in the amphitheater. Physicians and medical students are cordially invited to attend.

## HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held on Tuesday, October 8, in the amphitheater of the Peter Bent Brigham Hospital (Shattuck Street entrance) at 8:15 p.m. Dr. John Scudder, instructor of surgery, College of Physicians and Surgeons, Columbia University, will speak on the subject "Shock, Blood studies as a guide to therapy."

Medical students and physicians are cordially invited to attend.

## JEWISH MEMORIAL HOSPITAL

There will be a staff meeting of the Jewish Memorial Hospital in the hospital auditorium, 45 Townsend Street, Roxbury, on Monday, September 30, at 8 30 p.m. Dr. Reginald Fitz will speak on "Diabetes and the General Practitioner," followed by an open discussion. A collation will be served.

Physicians and medical students are invited.

## FOUR COUNTY MEDICAL SOCIETY

The annual meeting of the Four County Medical Society, comprising the district societies of Berkshire, Franklin, Hampden and Hampshire, will be held on Wednesday, October 9, at the Sheraton Hotel (formerly the Hotel Stonehaven), 70 Chestnut Street, Springfield. The meeting is scheduled for 9 30 a.m., luncheon will be served at the Sheraton Hotel at 1 00 p.m.

The meeting will be in the form of a symposium, "Dyspnea and Edema: Their significance in diagnosis and prognosis." Dr. Soma Weiss will discuss the viewpoint of general medicine, Dr. Edward D. Churchill, general surgery, Dr. Foster S. Kellogg, obstetrics and gynecology, and Dr. Burton E. Hamilton, cardiology.

All physicians of Western Massachusetts are welcome to attend.

SIXTH POSTGRADUATE SEMINAR  
IN NEUROPSYCHIATRY

The Metropolitan State Hospital, Waltham, recently announced the opening of the Sixth Postgraduate Seminar in Neuropsychiatry.

The course consists of two units—neurology, September 30 to December 17, and psychiatry, January 6 to March 24. It is designed as a comprehensive review course, not only for physicians preparing for the examinations of the American Board of Psychiatry and Neurology, but for those desirous of additional training in the specialty. The teaching staff comprises a number of recognized specialists in this field throughout the state and is under the direction of Dr. Roy D. Halloran, superintendent, Metropolitan State Hospital, and Dr. Paul I. Yakovlev, clinical director, Walter E. Fernald State School.

NEW ENGLAND SOCIETY  
OF ANESTHESIOLOGY

The next regular meeting of the New England Society of Anesthesiology will be held in the White Auditorium of the Massachusetts General Hospital on Monday, October 7, at 8 00 p.m. Dr. C. H. Robson, of Toronto, Canada, will speak on the subject "Anesthesia for Children."

UNITED STATES CIVIL SERVICE  
EXAMINATIONS

Junior Medical Officer (rotating internship) \$2000 a Year  
Junior Medical Officer (psychiatric resident) \$2000 a Year

Applications must be on file with the United States Civil Service Commission at Washington, D. C., not later than October 7.

For the rotating internship at St. Elizabeths Hospital, Washington, D. C., applicants must be fourth year students in a Class-A medical school, however, they cannot enter on duty until they furnish a certificate showing completion of the medical course prior to June 30, 1941.

For the psychiatric resident position at St. Elizabeths Hospital, applicants must have completed their fourth year of study in a Class-A medical school subsequent

to December 31, 1937, and must have the degree B.M. or M.D. In addition, before entrance on duty must have completed a one-year rotating internship.

Further information and the necessary forms may be obtained from the Secretary, Board of United States Civil Service Examiners, at any first-class or second-class office, or from the United States Civil Service Commission, Washington, D. C.

## SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING  
SUNDAY, SEPTEMBER 29

## MONDAY, SEPTEMBER 30

\*8 30 p.m. Diabetes and the General Practitioner Dr. Reginald Fitz  
Jewish Memorial Hospital 45 Townsend Street Roxbury

## TUESDAY, OCTOBER 1

\*9-10 a.m. Differential Diagnosis of Certain Diseases of the Skin  
Dr. J. D. Adams Joseph H. Pratt Diagnostic Hospital

## WEDNESDAY, OCTOBER 2

\*9-10 a.m. Hospital case presentation Dr. S. J. Thannhauser  
H. Pratt Diagnostic Hospital

\*12 m. Clinicopathological conference Children's Hospital.

## THURSDAY, OCTOBER 3

\*9-10 a.m. Cardiovascular clinic Dr. John Homan, Joseph H. Pratt Diagnostic Hospital

## FRIDAY, OCTOBER 4

\*9-10 a.m. Carcinoma of the Breast Dr. E. M. Daland, Joseph H. Pratt Diagnostic Hospital

## SATURDAY, OCTOBER 5

\*9-10 a.m. Hospital case presentation Dr. S. Thannhauser  
H. Pratt Diagnostic Hospital

\*Open to the medical profession

- SEPTEMBER 27-28—New England Surgical Society, Poland Spring, Me.  
OCTOBER 24—Forty First Annual Meeting of the American Roentgen Society, Page 478, issue of September 19.  
OCTOBER 6-11—Annual meeting of the American Academy of Ophthalmology and Otolaryngology, Page 81, issue of July 11.  
OCTOBER 7—New England Society of Anesthesiology, Notice above.  
OCTOBER 8—Harvard Medical Society, Page 655, issue of April 11.  
OCTOBER 8-11—American Public Health Association, Page 655, issue of April 11.  
OCTOBER 9—New England Dermatological Society, Page 390, issue of September 5.  
OCTOBER 9—Four County Medical Society, Notice above.  
OCTOBER 10—Pentucket Association of Physicians, Page 369, issue of February 29.  
OCTOBER 11-12—Pan American Congress of Ophthalmology, Page 369, issue of May 23.  
OCTOBER 14-25—1940 Graduate Fortnight of the New York Academy of Medicine, Page 305, issue of August 22.  
OCTOBER 21—American Board of Internal Medicine, Page 369, issue of February 29.  
NOVEMBER 13-14—New England Postgraduate Assembly, Cambridge, Massachusetts.  
DECEMBER 27-29—National Convention of the Association of Medical Students, Boston.  
JANUARY 4, 1941—American Board of Obstetrics and Gynecology, 1064, issue of June 20.  
MARCH 8—American Board of Ophthalmology, Page 201, issue of August 1.  
APRIL 21-25—American College of Physicians, Page 1065, issue of June 20.  
JUNE 2-6—American Medical Association, Cleveland, Ohio.

## DISTRICT MEDICAL SOCIETIES

## SUFFOLK

NOVEMBER 7—Cephares meeting, Page 305, issue of August 1940.  
WORCESTER

OCTOBER 9—Rutland State Sanatorium, Rutland.  
NOVEMBER 13—Grafton State Hospital, Grafton.  
DECEMBER 11—St. Vincent Hospital, Worcester.  
JANUARY 8, 1941—Worcester City Hospital, Worcester.  
FEBRUARY 12—Worcester State Hospital, Worcester.  
MARCH 12—Memorial Hospital, Worcester.  
APRIL 9—Hahnemann Hospital, Worcester.  
Supper will be served at 6 30 p.m. followed by a business and scientific program.

## BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished upon request.

*Textbook of Medicine*. By American authors. Edited by Russell L. Cecil A.B., M.D. Sc.D., professor of clinical medicine, Cornell University Medical College, attending physician, New York and Bellevue hospitals, New York City; associate editor Foster Kennedy M.D., F.R.S.E., professor of clinical neurology, Cornell University Medical College, attending physician, New York Hospital; visiting physician-in-charge, Neurological Service, Bellevue Hospital; consulting physician, New York Neurological Institute. Fifth edition revised and enlarged. 8, cloth, 1744 pp. with 173 illustrations. Philadelphia and London W. B. Saunders Company 1940.

*Care and Training*. By Marion L. Faegre, assistant director of parent education and John E. Anderson, director, Institute of Child Welfare, University of Minnesota. Fifth edition revised. 8, cloth 320 pp., with 29 illustrations and 3 tables. Minneapolis: University of Minnesota Press 1940 \$2.50.

*Heart Failure*. By Arthur M. Fishberg M.D., associate physician, Mount Sinai Hospital, New York City. Second edition, thoroughly revised. 8, cloth, 829 pp., with illustrations. Philadelphia: Lea & Febiger 1940 \$8.50.

*Progress in Medicine: A critical review of the last hundred years*. By Iago Goldston M.D. With a foreword by Henry E. Sigerist M.D. 8, cloth 361 pp. New York: Alfred A. Knopf 1940 \$3.00.

*Histamine and Insulin Treatment of Schizophrenia and Other Mental Diseases*. By Horace Hill M.R.C.P., medical superintendent, Laverstock House Mental Home, Surrey, England. 12, cloth 133 pp. Baltimore: Williams & Wilkins Company 1940 \$1.75.

*Clinical Diagnosis*. By Ralph H. Major M.D., professor of medicine, University of Kansas. Second edition revised. 8, cloth, 464 pp., with 437 illustrations. Philadelphia and London W. B. Saunders Company 1940 \$5.00.

*Creidulous and Genius*. By Lewis J. Moorman M.D. 8, cloth 272 pp. with 10 portraits. Chicago: University of Chicago Press, 1940 \$2.50.

*Introduction to Medical Biometry and Statistics*. By Raymond Pearl A.B., Sc.D., Ph.D., LL.D., professor of biology, School of Hygiene and Public Health and Medical School, Johns Hopkins University. Third edition revised and enlarged. 8, cloth with 171 illustrations and 140 tables. Philadelphia and London W. B. Saunders Company 1940 \$7.00.

## BOOK REVIEWS

*Dermatologic Allergy*. By Marion B. Sulzberger. 8, cloth 540 pp., with 39 illustrations, 13 colored plates and tables. Springfield, Illinois: Charles C. Thomas 1940.

Sulzberger has done an invaluable work in formulating a monograph on allergy. He presents a series of lec-

tures on dermatologic allergy given to postgraduate students; these contain an unusual amount of valuable information. The author states it is neither a book of reference nor an encyclopedia on allergy; nor is it intended for the expert, but is merely a primer or introduction to dermatologic allergy for the purpose of instructing beginners in this field. He makes no pretense that this monograph will qualify students to diagnose and manage allergic skin diseases. It is given with the hope that something of practical value may help to stimulate further thought and encourage additional studies and investigations. However, if the reader masters the knowledge contained in this book, he will be thoroughly cognizant of all recent research in this field. It consists of fourteen lectures and an appendix which gives a list of the substances used in patch testing with the concentrations which are innocuous to normal skins, an outline of treatment for eczematous and urticarial dermatoses and a useful glossary of technical terms. Each lecture can be rapidly summarized by the marginal notes.

The first table is a schematic presentation of some of the important forms of allergic sensitivity. It groups certain phenomena according to the etiologic factor and others according to the mechanism, a classification which he acknowledges is faulty. He remarks that his definition of allergy is a paraphrase or practically the translation of von Pirquet's original definition, and that the outstanding merit of the concepts of allergy lies in the demonstration of the closer relation of the phenomena of specific acquired increased sensitivity and those of specific acquired decreased sensitivity.

His definitions are clear and concise. He adheres faithfully to them and his constant repetition of his concepts of allergic phenomena leaves no doubt in the mind of the reader as to just what he believes. After reading this book, the reader will find himself a willing or an unwilling disciple, because such constant repetition is bound to fix these definitions in his mind. While he may not agree with all the author's ideas, he will look in vain for errors and statements that are not supported by experimental work.

The section concerning the steps in establishing certain dermatoses on the basis of allergy should be read by all allergists as well as by dermatologists. The first step—the establishment of the dermatologic diagnosis—is most important and requires dermatologic training. As he states, one frequently sees a patient with a non-allergic disease put through numerous unnecessary skin tests. The second step postulates that there must be a history of exposure to substances which will fill the requirements of being possible allergens in the particular case. Such a history eliminates unnecessary testing.

Each lecture dealing as it does with a particular phase of allergy and the investigation of the individual cases, is especially valuable in that it gives common sense procedure in the study of cutaneous manifestations. The various types of skin tests are described and evaluated and their advantages and disadvantages are clearly defined. The diagnosis of fungous diseases and the specific reactions to fungous extracts are discussed, so that the reader should obtain a working knowledge of the value of the latter in the diagnosis and treatment of these diseases. The chapter on drug eruptions emphasizes the role played by allergy in their production, describes recent research and lists the drugs known to cause dermatoses, the types of pathologic manifestations and the diagnosis and treatment. His comments expressed in footnotes are interesting and are based on his own experimental work for which he deserves great credit.

What is true of this book is also true of other books on allergy, one wonders why there is so much ado about the concept of allergy. The condition was originally proposed to include those concepts not adequately expressed under the term "immunity." If it continues to stimulate its adherents to further research in the determination of the etiologic factor of disease, it should be accepted by all physicians, but if it leads off into bypaths of theoretical conjectures, it would be better to continue with the more ancient terms which are at least entrenched in medicine, perhaps for no better reason than established custom.

While the reviewer recommends that this book be read by dermatologists and practitioners of medicine in general, he especially recommends it to those specializing in allergy who have not had a dermatologic training.

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*Virus and Rickettsial Diseases, with Especial Consideration of Their Public Health Significance. A symposium held at the Harvard School of Public Health, June 12-17, 1939* 8°, cloth, 907 pp, with illustrations and tables Cambridge Harvard University Press, 1940 \$6.50

The purpose of the comprehensive symposium held at the Harvard School of Public Health in June, 1939, is succinctly stated in the preface of this volume, "To furnish an opportunity for the presentation and discussion of those problems of infectious disease in which virus agents are involved." "Publication," it is stated, "was undertaken because it was hoped that at the present state of virus investigation—a stage which we may regard as merely the beginning of an era in medicine which already equals in importance the most brilliant period of modern bacteriology—a contemporaneous survey might be found useful."

The growth of knowledge concerning both virus and rickettsial diseases during the past ten years has so outstripped the experience of the average health officer and of the practitioner interested in this field that such a summary is indispensable for the worker who attempts to maintain the vital line of communication between the basic sources of information and the rapidly widening fields of application. The investigator will look here chiefly for well annotated statements of established facts and principles, the epidemiologist or health officer, on the other hand, will turn to it repeatedly as an encyclopedia which enables him to retain his perspective in the changing picture of communicable-disease control.

The limits of a book review preclude detailed discussion of particular subjects, but for the clinician the classification and consideration of the virus encephalitides offer a working approach, and the chapter on equine encephalomyelitis is a timely summary of our knowledge of a disease apparently new to the eastern seaboard of the United States.

The inclusion of rickettsial diseases in the symposium is pertinent because of their former confusion with virus diseases, because of their public-health significance and because of the recent notable additions to our knowledge of their epidemiology and immunology, especially in connection with typhus fever.

The inclusion of a chapter on distemper in animals may be criticized as not pertinent to a consideration of the virus diseases of man, but it should be remembered that the observation and study of a spontaneous infection in ferrets laid the foundation for practically all the recent advances in our knowledge of influenza. It is hard to see how the role of reporting in the control of measles has any specific bearing on its characteristics as a virus disease. Certainly the administrative questions which the

author sets for himself involve no etiologic problem. These are not equally pertinent to the control of whooping cough or scarlet fever.

Aside from its excellence as a compendium of diseases the volume is notable in being the work of a faculty and former students of a single university. Certain aspects of the subject, it is true, were conscientiously treated, but as a result a large part of the material is original work of the authors. Although intended for the general student and health officer, the book provides a comprehensive bibliography for the reader who wishes to penetrate more deeply into any of the various fields which he is interested in.

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*Good Health and Bad Medicine* Harold Aarseth 8°, cloth, 328 pp New York Robert M. McEldowney Company, 1940 \$3.00

The modern conception of the most effective method of a general health campaign lies, first, in the educated medical profession and, second, in an informed citizenry who know what is true or false in the propaganda employed in dealing with the prevention and treatment of illness.

The obstacles in the way of bringing about the adoption of the recommendations of those who see the advantage to the individual and the nation of sound minds in healthy bodies consist in the subversive propaganda for the maintenance of the cults on the one hand, and the corresponding interest engaged in the distribution of worthless and dangerous drugs or appliances on the other.

Although Congress has enacted the Food, Drug, and Cosmetic Act designed to protect the health and interests of the people, this legislation is far from adequate, more effective correction of the situation lies in the education and inclination of the public to discriminate between the good and the harmful, advertised products.

The book is a valuable and supplementary contribution to the campaign carried on by organized medicine. Each chapter is a model of concise and well-arranged statements dealing with the disorders of the organs and systems of the human body. Especially valuable is the chapter devoted to emergencies, with directions about what to do before the doctor arrives when one has to deal with serious accidents or ingested poisons.

Physicians will find in this publication informal arguments which may be useful in combating ignorance and prejudice.

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*The New International Clinics* By George Morison, M.D. Vol. I, New Series 3 8°, cloth, 319 pp 31 illustrations Philadelphia J. B. Lippincott Co. 1940 \$3.00

This volume is particularly broad in scope, embracing articles of great diversity. The subjects are far from stereotyped, as evidenced by "An Operation for the Removal of Certain Intractable Corns Between the Fourth and Fifth Toes," "Nail Cracks in Diabetes," and clinics on "The Synergism of Human Influenza Virus and Staphylococcus aureus in a Rapidly Fatal Respiratory Infection," "Cerebral Migraine," "An important form of 'angina pectoris,'" and "Relief of Pain in Cancer of the Tongue and Pharynx." An unusual feature of the book is the exceptionally large number of articles written with the efforts of two contributors. A long review on the subject closes a volume of high standard.

